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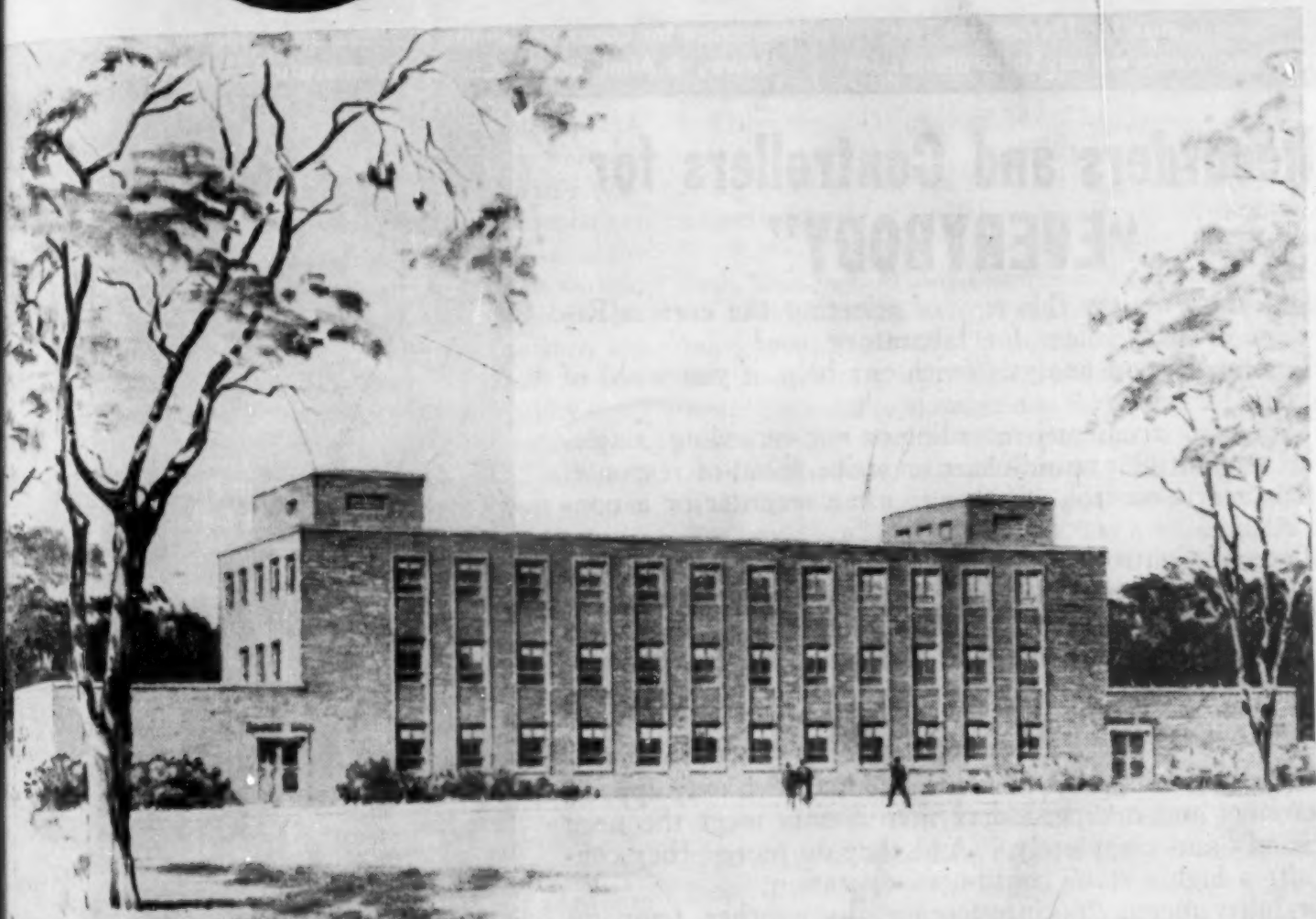
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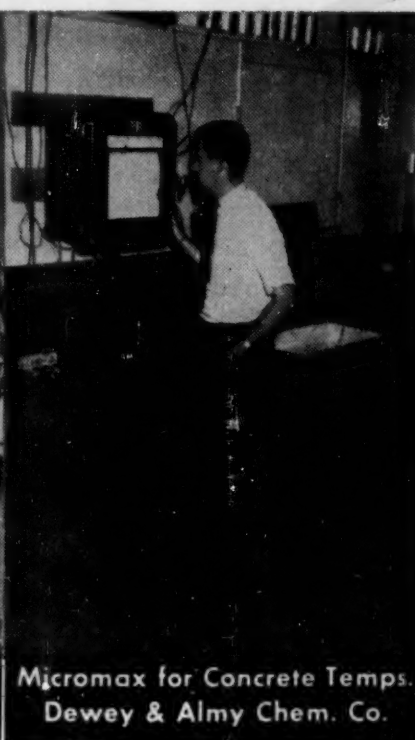
Savage Hall, new headquarters of Cornell University's School of Nutrition, being dedicated today at a convocation entitled "Nutrition—A Key to Human Welfare." The new \$500,000 structure, named in honor of the late Elmer Seth Savage, a pioneer in nutrition at Cornell and a member of its faculty for 35 years, was financed by farmers of the Northeast; the equipment was provided by the State of New York.

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Genetic Effects of the Atomic Bombs  
in Hiroshima and Nagasaki



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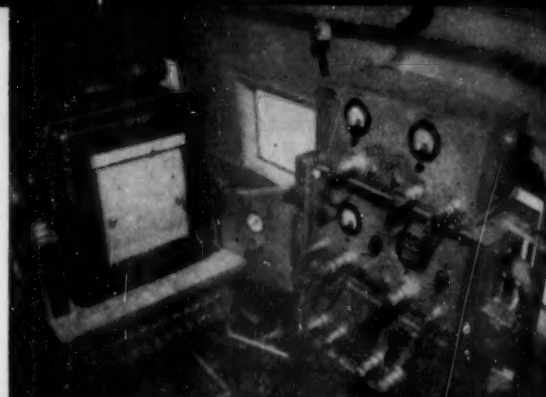
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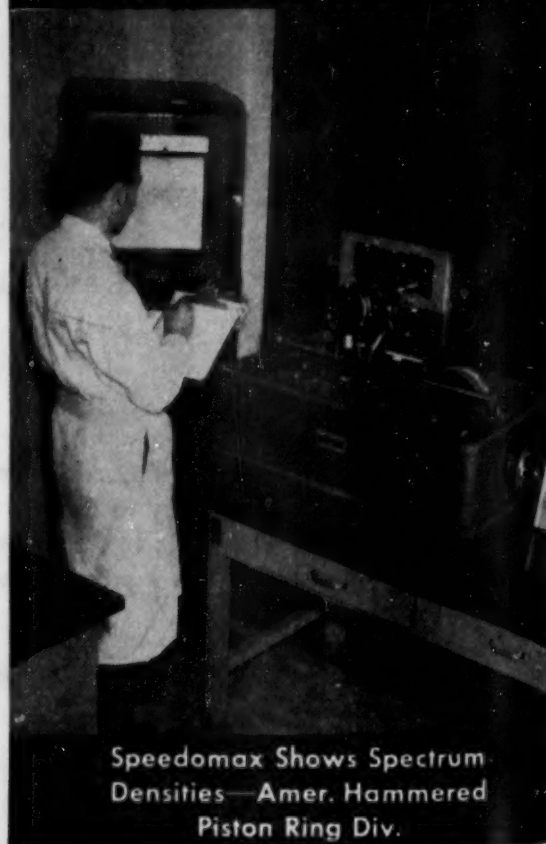
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# Genetic Effects of the Atomic Bombs in Hiroshima and Nagasaki

*Genetics Conference, Committee on Atomic Casualties, National Research Council*

The Atomic Energy Commission recently formally signified its intention of supporting long-range medical studies of the survivors of the atomic bombings in Japan, to be conducted by the Committee on Atomic Casualties of the National Research Council. One aspect of these studies will concern the much-discussed potential genetic effects of the bombs. The background of this program begins shortly after Japan's surrender, when a Joint Army-Navy Commission made extensive observations in Hiroshima and Nagasaki on the survivors of the bombings. At the conclusion of the Commission's work its chairman, Col. A. W. Oughterson, M.C., AUS, recommended to the Surgeon General of the Army that the Council be requested to undertake a long-range study of the medical and biological effects of the atomic bomb, and this recommendation was transmitted by Surgeon Gen. Norman T. Kirk to Lewis H. Weed, chairman of the Division of Medical Sciences. As a result, in June 1946 a conference group was convened by the Council, and in November, following its recommendation, a five-man commission composed of representatives of the Council, the Army, and the Navy left for Japan for the purpose of determining the current status of Japanese work on atomic bomb casualties, evaluating the feasibility of American participation in continued research on these casualties, and indicating the lines along which such studies should proceed. This commission, known as the Atomic Bomb Casualty Commission and composed of Austin Brues, Paul S. Henshaw, Lt. Melvin Block, M.C., AUS, Lt. James V. Neel, M.C., AUS, and Lt. (j.g.) Frederick Ullrich, (MC) USNR, submitted a report of its findings to the Council in January 1947.

The June 1946 conference group had recommended that appropriate action be taken to obtain a Presidential Directive

authorizing the National Research Council to initiate a long range study of the atomic bomb effects. This Directive was issued at the request of the Secretary of the Navy, James T. Forrestal, in November 1946, and on its authority the Council, in January 1947, established a Committee on Atomic Casualties, composed of Thomas M. Rivers (chairman), George W. Beadle, Detlev W. Bronk, Austin Brues, George M. Lyon, C. P. Rhoads, Shields Warren, Stafford L. Warren, George H. Whipple, and Raymond E. Zirkle.

The potential genetic effects of the atomic bomb were apparent to all interested students from the day the first bomb was dropped—in fact, to some, well before that time. A consideration of genetic studies was one facet of the work of the Atomic Bomb Casualty Commission, and a section of its January 1947 report was devoted to this subject. This phase of the work was to a large extent the responsibility of Lt. James V. Neel.

On June 24, 1947, the Committee on Atomic Casualties arranged a conference on the potential genetic effects of the atomic bombs. At this meeting, which was attended by George W. Beadle (chairman), Donald R. Charles, Charles H. Danforth, Herman J. Muller, Laurence H. Snyder, and Lt. Neel, the latter submitted a report of preliminary genetic studies, based on his observations in Japan during the preceding six months. Following a thorough appraisal of the problem, the conference voted to recommend to the Committee on Atomic Casualties that a program be undertaken in Japan along the lines sketched out in the Neel report. This recommendation was accepted at a meeting of the Committee on June 26, 1947. The conference also recommended that a statement be prepared, briefly summarizing the current status of the problem. This statement follows.

**W**HETHER THE ATOMIC BOMBS dropped on Hiroshima and Nagasaki will have detectable genetic effects on the Japanese is a question of widespread interest. The purpose of the present note is to show briefly that (1) many difficulties beset any attempt to obtain a valid answer to this question and (2) even after a long-term study, such as that outlined below, it still may not be possible to determine just how much genetic damage was done at Hiroshima and Nagasaki.

This memorandum is essentially a partial summary of the material presented by Lt. James V. Neel at the meeting of the Conference on Genetics convened by the Committee on Atomic Casualties of the National Research Council on June 24, 1947, but with certain additional considerations which grew out of the deliberations of the Conference.

It must first be recognized that, inasmuch as the majority of mutations occurring in animals are recessive,

only the relatively small proportion of mutations which are dominants may be expected to show effects in the first postbomb generation. The potential range in their effects is very wide. Dominant mutations with large, clear-cut manifestations can be expected to be much rarer than those with smaller, but possibly quite significant, effects on bodily dimensions, life span, etc. But the detection of these latter is a matter of great difficulty with present techniques. For practical considerations investigation will have to be concentrated chiefly on the class with such large effects as may lead to stillbirths, to live births with gross external abnormality, or to internal defects causing death or serious illness in infancy.

Since there is no general agreement as to what proportion of cases of abnormal fetal development is genetically determined, and what proportion is due to nongenetic factors, an increased incidence of morphologically abnormal fetuses following irradiation may not be used as an index of the frequency of genetic change until the non-

genetic effects of this irradiation on the reproductive history of the mother have been determined. This point will be very difficult to evaluate.

It is obvious that in this case the approach to the problem of genetic effects is the statistical one. It is unlikely that any individual and specific pathology in a post-irradiation generation can ever be attributed with certainty to the effects of the bomb, but if there is a definite increase in the occurrence of abortions, miscarriages, stillbirths, and abnormal products of conception, one may surmise that this is related to the bombing—although some of the effects need not necessarily be genetic. Appropriate control studies in other Japanese cities are therefore of the utmost importance.

The survivors of the bombing received amounts of irradiation ranging from negligible to just short of lethal. It is impossible to say on a priori grounds whether an adequate number of people absorbed sufficient radiation to produce enough dominant mutations to result in detectable effects. However, comparison of this situation with the experimental data on infrahuman material suggests that these effects, if detectable, will be small. The median lethal dose for whole body irradiation in man is probably in the neighborhood of 500 Roentgen units (Shields Warren. *Physiol. Rev.*, 1944, **24**, 225-238). It is likely that many individuals in Hiroshima and Nagasaki who received high but sublethal doses of irradiation sustained other injuries which, in combination with the radiation damage, resulted in death. Thus, the mean radiation dose received by the surviving population will be lower than expected from a consideration of the median lethal dose alone. In terms of radiation genetics this is a small exposure, expected from data on animals to produce a frequency of dominant mutations which would increase the normal frequency of abnormal offspring by so small a proportion as to be difficult to demonstrate. Large-scale studies, utilizing all available material, plus accurate vital statistics, are thus necessary if data of value are to be obtained. In this connection it is important to bear in mind that the available children born to parents who received significant amounts of irradiation will probably not exceed 12,000 or 13,000 within the next 10 years.

The Japanese had recognized the importance of genetic studies and, under great difficulties, were organizing a program in Hiroshima when the Atomic Bomb Casualty Commission arrived. They had planned to compare the present and future frequency of abnormal births in Hiroshima with the frequencies reported in their medical literature and vital statistics during the prewar years. But it is by no means sure either that the prewar figures were sufficiently accurate or that the present reporting of vital statistics would be wholly effective in detecting rare effects of the atomic bomb radiations. It cannot be too strongly emphasized that there is at present absolutely no reliable evidence on which to base any opinion

concerning the absolute or relative frequency of congenital abnormalities among children being born in Hiroshima and Nagasaki. Unfortunately, a good deal of misinformation is currently in circulation.

Two independent programs, one Japanese and one American, would involve needless duplication of effort. A joint undertaking is therefore indicated. In view of the fact that the Japanese are actively attempting to initiate genetic studies, it seems that any American efforts which may materialize should contemplate cooperation with the Japanese in an attempt to ensure an efficient and satisfactory program. The Neel report contains the following seven specific recommendations as to the organization of a program:

- (1) Organize, in Hiroshima, Nagasaki, and a control area or areas, a modified system of pregnancy registration, this to include the irradiation history of the parents.
- (2) Obtain as complete information as possible on the outcome of each registered pregnancy.
- (3) Follow up each report of an abnormal termination of pregnancy or a congenital malformation with detailed family studies.
- (4) Develop a system of checking on the completeness and accuracy of registration of births and deaths, such as requiring at intervals dual registration by both the family and the obstetrician or midwife.
- (5) Conduct these studies on a sufficiently large scale that the results will have statistical significance.
- (6) Integrate this program with a system of periodic examination of the offspring of irradiated persons and with careful death certification, so that genetic effects not apparent at birth but detected subsequently may be recorded. In particular, causes of infant mortality should be accurately recorded.
- (7) Place this program in competent Japanese hands, through the Japanese Government, with only enough American supervision and cooperation, including supplies, to facilitate a successful program.

This program must extend over a period of 10-20 years before a significant amount of data can be accumulated, and quite possibly an even longer period of study, extending to the second and subsequent generations, will be indicated.

Certain practical limitations of the program may be considered at this point. The most difficult problem will be to obtain the necessary completeness of reporting. This will require constant effort, a wide educational program, and frequent cross-checks. Congenital malformations occurring within Japanese families may sometimes not be reported. This is perhaps more likely to occur in Japan than in this country, because probably less than 10 per cent of Japanese births occur in hospitals as these are defined in the United States. To what extent stillbirths and malformations occurring outside a hospital will be recorded depends on the vigor with which the problem is pursued. It will be difficult to get evenly matched teams of investigators for bombed and control areas. Furthermore, once people living in Hiroshima and



Nagasaki learn that stillbirths and malformations may possibly be attributed to the effects of the bomb, they will probably lose some of their reluctance to report such matters, whereas this will not be the case in a control area.

Japan is now a defeated and occupied country, under severe postwar stress, whose people have a very different psychology from our own. A program such as that under consideration will proceed much more slowly here than it would in this country.

In order to reduce the possibility that a negative result of the investigation on Japanese material be interpreted by the medical and lay public as meaning that important genetic effects were not produced, it is essential that a comparable effort be expended in experimentation on other mammalian material, in which genetic effects of different kinds can much more readily be brought to light. In this way it should be possible to throw light upon the proportion of the total genetic

effects produced by the radiation that would have been detectable by the methods used in the investigation on the human material, and the serious danger of misinterpretation of the latter results would be minimized.

Recognizing the difficulties briefly touched upon in the foregoing paragraphs, the Conference on Genetics voted unanimously to record the following expression of its attitude toward the genetic program: "Although there is every reason to infer that genetic effects can be produced and have been produced in man by atomic radiation, nevertheless the conference wishes to make it clear that it cannot guarantee significant results from this or any other study on the Japanese material. In contrast to laboratory data, this material is too much influenced by extraneous variables and too little adapted to disclosing genetic effects. In spite of these facts, the conference feels that this unique possibility for demonstrating genetic effects caused by atomic radiation should not be lost."

## An Auditory Afterimage?

W. A. Rosenblith, G. A. Miller, J. P. Egan,  
I. J. Hirsh, and G. J. Thomas

*Psycho-Acoustic Laboratory, Harvard University*

FOR THOSE WHO LIKE TO EMPHASIZE THE similarities between our different sense modalities, the absence of auditory afterimages has been a persistent puzzle, a blank in the table of analogies which can be drawn between vision and audition. There is, of course, tinnitus—that annoying ringing in the ears that often follows exposure to deafening sounds. But tinnitus may last for hours, is often pathological in origin, and resembles "spots before the eyes" more than a true afterimage. Tinnitus excluded, therefore, the story of unrewarded searching (1) seems to justify the conclusion that auditory afterimages do not exist.

The error of such a conclusion can be demonstrated with the help of a pulse generator and a pair of earphones. The generator is used to produce a train of rectangular voltage pulses at a rate of about 100 pulses per second. The rectangular pulses used in this experiment contain all harmonics of the fundamental pulse repetition frequency at approximately equal amplitude over the frequency range transmitted by the earphones (cutoff around 6,500 cps). The earphones transduce the voltage pulses to acoustical pulses, and the listener is allowed to hear this buzzing sound at a high intensity for one or two minutes. When the earphones are removed, there is a striking change in the timbre of such familiar sounds

as a handclap, a typewriter, the voice, etc. A peculiar metallic quality seems to be added to the sounds. Listeners have described the sounds as "jangly," "twangy," "like a rasping file," or "like two pieces of iron being rubbed together." The aftereffect of the pulses is transient, and in a few seconds the sounds regain their normal quality.

We have had no trouble in demonstrating this aftereffect to subjects with normal hearing. It has been experienced in reverberant and anechoic rooms, with test noises produced in the room, over a loud-speaker, or in headphones. Phonographically recorded handclaps, sibilant consonants, the sound of scraping sandpaper, and typewriter noises seem to work about as well as the original sounds themselves.

Several questions immediately suggest themselves. What characteristics of the exposure stimulus are necessary to produce the effect? What kind of test stimuli can be used? What is the quality and duration of the effect?

Exposure to intense random noise—a hissing sound—is ineffective in producing the aftereffect. Random noise interrupted at regular intervals to give a train of 150 bursts of noise per second was also a failure. Nor did a combination of 11 oscillators producing frequencies not in harmonic relation elicit the aftereffect. Very loud pure tones of low frequency may evoke the phenomenon for some listeners. A square wave elicits the aftereffect but is much less impressive than the pulses. Pulses produce

The research described in this paper was carried out under contract with the U. S. Navy, Office of Naval Research (Contract N5ori-76, Report PNR-39).

the phenomenon even when they are modulated in frequency from about 100 to 200 pulses per second at a rate of 20 times each second or when the low-frequency components of the spectrum are filtered out of the pulses. With a pulse repetition frequency of 140 pps the aftereffect was obtained when only those component frequencies of the pulse between 3,120 and 4,000 cps were passed, and again when only the range between 4,000 and 6,600 cps was heard. When only the first 4 harmonics of the pulse—140, 280, 420, and 560 cps—were used as the exposure stimulus, the effect was not observed, and not until the first 10 harmonics were passed was a clear after-

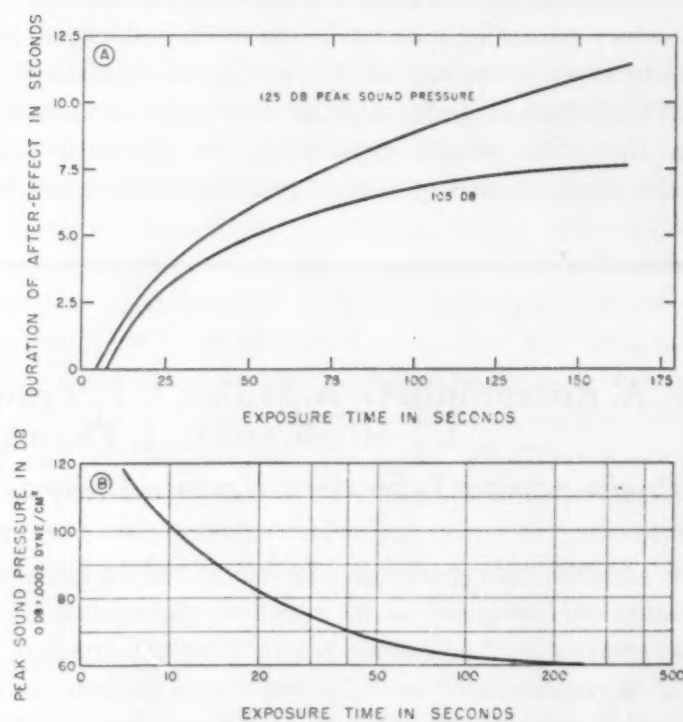


FIG. 1. A—Duration of aftereffect as a function of exposure time (parameter: peak sound pressure; pulse repetition frequency = 120). B—Peak sound pressure vs. exposure time for fixed duration of aftereffect (2 seconds) (pulse repetition frequency = 140).

effect obtained. It seems that the high-frequency components of the pulse are necessary for the phenomenon to occur, but it is not clear whether these frequencies are necessary because they stimulate a certain portion of the basilar membrane or because they preserve the sharp onset of the pulses.

The pulses used were of 120-microsecond duration, and the instantaneous sound pressure at the peak of the pulse was varied from approximately 75 to 125 db re 0.0002 dyne/cm.<sup>2</sup> For convenience in exploring the phenomenon the following procedure was adopted: The sound of two pieces of sandpaper being rubbed together at a regular rate was phonographically recorded, and the listener was exposed to the train of pulses for a fixed period of time at a given intensity and pulse repetition frequency. At the end of the exposure the experimenter switched to the phonograph channel, the listener being allowed to hear the sound of scraping sandpaper. The listener's task was then to count the number of scrapes of the sandpaper which seemed to be "metallic" in quality. By converting

sandpaper rubs to a more conventional time base, the duration of the afterimage was given for the conditions of stimulation.

Durations of exposure between 5 and 240 seconds were explored, the longer exposures producing the most marked aftereffects. When the sound pressure at the peak of the pulse was held constant, the duration of the aftereffect increased as a negatively accelerated function of the exposure time. This is illustrated in Fig. 1A for two intensity levels. Fig. 1B shows the peak sound pressure necessary to elicit an aftereffect of constant duration (2 seconds). To a certain degree, exposure time can be substituted for exposure intensity. As a practical matter, an exposure of 20 or 30 seconds represents a convenient compromise between the listener's impatience and the experimenter's desire to produce a measurable effect

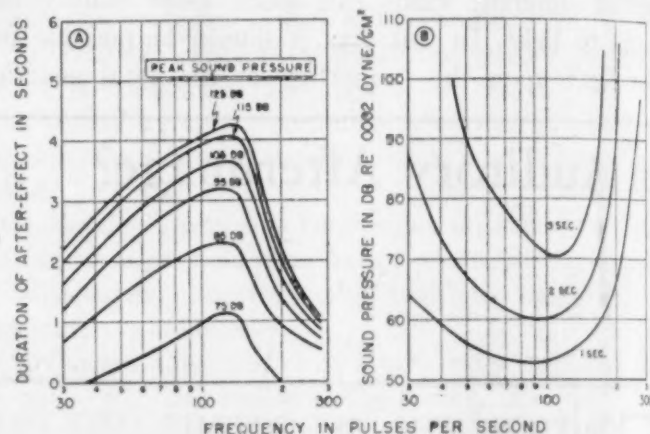


FIG. 2. A—Duration of aftereffect vs. pulse repetition frequency (parameter: peak sound pressure; exposure time = 20 seconds). B—Sound pressure vs. pulse repetition frequency (parameter: duration of aftereffect).

Only a narrow range of pulse repetition frequencies elicits the aftereffect. Frequencies between 30 and 200 pulses per second seem most effective. This is illustrated in Fig. 2A, where the duration of the aftereffect is plotted as a smoothed function of the pulse repetition frequency, with the peak pressure of the pulses as the parameter. These curves were obtained with three listeners and a constant exposure time of 20 seconds. In Fig. 2B the curves are replotted to show the intensity required to produce a given duration of the aftereffect.

A variety of test stimuli was tried, and the necessary attributes of a good stimulus seem to include familiarity to the listener, complexity in harmonic composition, and temporal discontinuity. Unfamiliar stimuli leave the listener wondering whether or not the test stimulus sounds as it should sound. Pure tones were poor so long as they were continuous; when they were interrupted, the effect was heard following the "click" of the interruption. Silence is silent: without a test stimulus our listeners report only a transient, impalpable, nonauditory awareness that an aftereffect persists. The dissipation of the aftereffect seems to be a function of time only and is independent of stimulation. For example, if an exposure normally produces an aftereffect lasting about 3 seconds,



2-second silence before the presentation of the test stimulus is followed by about 1 second of the aftereffect, and after a silent delay of 4 seconds no qualitative changes are observed.

The quality of the aftereffect does not seem to change as a function of the nature of the stimulations which produce it. It is always the same—a metallic, ringing obligato to the test stimulus.

What possible mechanism could account for this phenomenon? It seems to be peripheral, for if the left ear is exposed to pulses and the right ear is tested with the scraping of sandpaper, no aftereffect is experienced. It is probably related to stimulation deafness, but in no simple manner, since exposures only to certain kinds of sounds are followed by the aftereffect. Furthermore when, a temporary hearing loss produces a qualitative change in a test stimulus, we expect the change to be less pronounced for loud test stimuli, since the temporarily

deafened ear is more nearly normal in response to loud than faint sounds. The ringing auditory quality of the aftereffect is, however, most striking and persistent when the test stimulus is made more intense. The mechanism is more complex than a simple subtraction—due to hearing loss—of certain components of the test sound. Either a sharp wave-front or the presence of harmonics properly spaced along the basilar membrane is the necessary condition for producing it. In a highly mechanical system like the ear the possible mechanisms for an afterimage are somewhat limited.

Such, then, is the phenomenon observed. It is not a tinnitus, a simple hearing loss, or a pathological condition. It is a positive aftereffect of the stimulation of normal listeners. Is this not an auditory afterimage?

#### Reference

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## NEWS and Notes

**K. A. Gunnar Strand**, formerly associate professor of astronomy, University of Chicago, is the new director of the Dearborn Observatory and professor of astronomy, Northwestern University. Dr. Strand, a positional astronomer who did research in navigation for the Army Air Forces during the war, succeeds **Oliver J. Lee**, who had been on the Northwestern faculty since 1928 and who retired August 31. Dr. Strand received his Ph.D. degree from the University of Copenhagen, and came to the United States as a fellow of the American Scandinavian Foundation. His first assignment here was at Sproul Observatory, Swarthmore College. His studies have included the motion of asteroids, determination of position, photographic and visual observations of double stars, and orbital motion in multiple systems. He has been retained as a special research associate at Yerkes Observatory.

**Abraham White**, associate professor of physiological chemistry, Yale University School of Medicine, will deliver the first Harvey Lecture of the current series at the New York Academy of Medicine, October 23. Dr. White will speak on "Influence of Endocrine Secretions on the

Structure and Function of Lymphoid Tissue."

**Nathan Birnbaum**, Department of Chemistry, City College of New York, has returned to the Department after 5 years of military service with the Chemical Corps, U. S. Army. In addition to overseas duty in New Guinea and the Philippines, Prof. Birnbaum participated in the atomic bomb tests at Bikini as a member of the Radiological Safety Section. He is being retained by the Chemical Corps as consultant to the Research and Engineering Division.

**James G. Miller**, chief, Clinical Psychology Section, Neuropsychiatric Division, Veterans Administration, Washington, D. C., has been appointed chairman, Department of Psychology, University of Chicago. The appointment, which is effective January 1, 1948, carries the rank of professor of psychiatry and psychology. As a captain in the Army Medical Corps during the war, Dr. Miller served as a neuropsychiatrist, assessing personalities of OSS personnel both in this country and in the European Theater.

**Charles C. Price**, head, Department of Chemistry, University of Notre Dame, is now in England, where he will deliver a series of special lectures at Oxford, Cambridge, and other colleges and universities in England and Scotland. Dr. Price will also visit the Imperial Chemicals Industries at Manchester and the British Rubber Producers Association at Welwyn Garden City.

**Byron Clark** has assumed his duties as professor of pharmacology, Tufts College Medical School. Under his direction the laboratories for instruction and research in this field will be reorganized and enlarged.

**John H. Melvin**, district geologist, Corps of Engineers, Omaha, Nebraska, has been appointed state geologist of Ohio, succeeding **George W. White**, who has been appointed head, Department of Geology, University of Illinois.

**Samuel Cate Prescott**, of Cambridge, Massachusetts, former dean, School of Science, Massachusetts Institute of Technology, was awarded the honorary D.Sc. degree by Lehigh University at its 69th Founder's Day exercises, October 1.

**A. C. Ivy**, vice-president of the University of Illinois for the Chicago Professional Colleges, has been named an honorary member of the American Congress of Physical Medicine in recognition of his "studies of electrical stimulation of paralyzed muscles and resuscitation from carbon monoxide asphyxia, and for assistance to the Council of Physical Medicine of the American Medical Association."

**William J. Eney**, professor of civil engineering, Lehigh University, has been appointed head, and director of the curriculum, Department of Civil Engineering. He succeeds **Hale Sutherland**, who will continue as professor in the Department and will devote more of his time to professional writing.

**D. T. Morgan, Jr.**, has been appointed assistant professor of botany, University of Maryland.

**Carl G. Hartman**, professor emeritus of physiology and zoology, University of Illinois, has recently been appointed director of physiology and pharmacology, Ortho Research Foundation, Raritan, New Jersey.

**Mark W. Woods**, associate professor of plant pathology, University of Maryland, has recently resigned to join the staff of the National Cancer Institute, Bethesda, Maryland.

**Morris T. James**, formerly assistant professor in entomology, Colorado Agricultural and Mechanical College, Fort Collins, has been appointed assistant professor of entomology, State College of Washington, Pullman.

**Jacob Sacks**, formerly pharmacologist, Endo Products, Inc., has been appointed to the staff of the Department of Biology, Brookhaven National Laboratory, Upton, New York.

**Herman C. Lichstein**, formerly National Research fellow, Cornell University, has been appointed associate professor of bacteriology, University of Tennessee, Knoxville.

**Emily T. Wolff**, formerly research botanist at the laboratories of the American Cyanamid Company, Stamford, Connecticut, has been appointed assistant professor of botany, University of Georgia, Athens.

**William M. McGill**, assistant state geologist of Virginia since 1929, was appointed state geologist, effective September 1, succeeding **Arthur Bevan**, now with the Illinois Geological Survey.

**Myron C. Benford**, head, Outpatient Department, University of Illinois Hospitals, has been promoted to assistant medical director to assist **John B. Youmans**, dean, College of Medicine and medical director of the hospitals.

**Joseph Modrovsky**, design engineer, Wright Aeronautical Corporation, Paterson, New Jersey, has been appointed assistant professor, Department of Mechanical Engineering, Polytechnic Institute of Brooklyn.

**Frank M. Semans**, consulting biologist, and formerly of Hiram College, has been appointed associate professor in biology, Arizona State College, Tempe.

**Charles A. R. Connor**, associate physician in cardiovascular disease and assistant chief, Cardiovascular Clinic, Lenox Hill Hospital, cardiologist, New York City Department of Health, and attending consultant, Veterans Administration, New York City, has been appointed medical director, American Heart Association, to succeed **David D. Rutstein**, who recently resigned to become professor of preventive medicine, Harvard Medical School.

**William Owens**, professor of psychology, Iowa State College, has been appointed head, Department of Psychology. During the war Dr. Owens served with the Standards and Curriculum Division, Bureau of Naval Personnel.

**S. Richard Silverman**, administrative executive, Central Institute for the Deaf, has been appointed director of the Institute, filling the position left vacant in 1941 by the death of **Max A. Goldstein**, who founded the Institute in 1914.

**F. J. Alcock**, formerly senior geologist, Geological Survey, Mines and Geology Branch, Department of Mines and Resources, Canada, has been appointed chief curator, National Museum, Ottawa.

**Lester W. Sharp**, professor of botany, Cornell University, retired from active service in the Department on July 1.

**A. W. Swensen**, professor of chemistry, and **Elmer W. Hertel**, professor of biology, have been promoted to full professors at Wartburg College, Waverly, Iowa.

**Milton Tinsley**, instructor in neurological surgery, University of Illinois, has been promoted to assistant professor. Dr. Tinsley joined the Illinois faculty in 1940.

**Joseph H. Greenberg** and **John M. Roberts** have been appointed assistant professors, Department of Anthropology, University of Minnesota, and **Ralph P. Winchester** has been appointed an instructor in anthropology in the General College of that University.

**Matilda Moldenhauer Brooks**, research associate, University of California, has returned from a summer's work in Peru, where she conducted experiments in the high Andes on overcoming altitude sickness. This work was carried out with the cooperation of C. Hurtado, minister of public health, Peru, and a group of medical men.

**Sunder Lal Hora** of India, a leading ichthyologist, has been appointed permanent director of the Zoological Survey of India, Kaiser Castle, Benares Cantonment, according to a letter received from him. **E. W. Gudger**, American Museum of Natural History, New York.

**Albert S. Cahn**, who served during the war as mathematician and physicist with a unit of the Manhattan Project at the University of Chicago, has been appointed executive officer of the Institute of Numerical Analysis, which is being established by the National Bureau of Standards on the campus of the University of California at Los Angeles.

**Cecil J. Watson**, professor of medicine, University of Michigan Medical School, will address the Institute of Medicine of Chicago and the Chicago Society of Internal Medicine, October 24, at the Palmer House, Chicago, on the topic "Some Aspects of the Porphyrin Problem in Relation to Disease."

### Visitors to U. S.

**L. C. Young**, of the mathematics research faculty, University of Cape Town, South Africa, is in the United States to direct research seminars in mathematics at Ohio State University during the 1948-49 autumn and winter quarters.

**Chentze Hsiang Wu**, assistant professor of physiology, National Central University Medical College, Nanking, China, who has been working with **Marice B. Visscher**, of the University of Minnesota Medical School, Minneapolis, since September 1946, is returning to Nanking this month. Dr. Wu has also been acting as a representative of the Natural Science Society of China to arrange publication exchanges for the Society.

### Grants and Awards

The School of Mathematics of the Institute for Advanced Study will allocate a small number of stipends to gifted young mathematicians and mathematical physicists to enable them to study and do research work at Princeton during the academic year 1948-49. Candidates must have given evidence of ability in research comparable at least with that expected for the Ph.D. degree. Application blanks, which may be obtained from the School of Mathematics, Institute for



anced Study, Princeton, New Jersey, returnable by February 1, 1948.

**The New York Zoological Society**, administrator of the New York Aquarium and its laboratories, has received grants from the National Advisory Cancer Council of the National Cancer Institute totaling \$15,088 for continuing the Aquarium's studies of melanomas in fish and amphibians. Research on the genetics and biology of normal and neoplastic pigment cell growth in fishes, initiated by **Myron Gordon**, geneticist, is now being expanded in cooperation with **F. Nigrelli**, pathologist, New York Aquarium. **V. V. Brunst**, formerly director, Laboratory of Roentgen Biology, Roentgen and Cancer Institute, is now senior fellow, National Institute of Health, will work on regeneration and transplantation of melanotic cells in the Mexican axolotls, a colony which is being established in the Genetics Laboratory of the Aquarium.

**Ell Liebman**, formerly research fellow, Department of Biology, Princeton University, will study the hematological and biochemical changes in progressive stages of normal, pretumorous, and melanomatous fishes. **William and Margaret Ardsen Tavalga**, graduate students, New York University Graduate School of Arts and Sciences, Department of Biology, are working on the embryological and endocrinological aspects of the problem. Dr. Gordon is coordinating the fire project at the Genetic Laboratories, temporarily located in the Whitney Wing, American Museum of Natural History.

**George W. Merck**, president, Merck & Company, Rahway, New Jersey, who directed the Nation's extensive research on biological warfare during World War II, will be awarded the Chemical Industry Medal for 1947 by the American Section, Society of Chemical Industry, at a dinner November 7, at the Hotel Commodore, New York. Mr. Merck was cited for "outstanding accomplishments" by Merck & Company in the field of pharmaceuticals, under his leadership.

**Joseph Aronson**, U. S. Bureau of Indian Affairs, received the Alvarenga Prize July 14 from the College of Physicians of Philadelphia in recognition of his studies on the evaluation of BCG vaccine in the control of tuberculosis. This prize was established by the will of Pedro Francisco da Costa Alvarenga, of Lisbon, Portugal, an associate fellow of the College of

Physicians, "to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883." The College usually makes this award for outstanding work and invites the recipient to deliver an Alvarenga Lecture before the College.

**The Spirit of St. Louis Medal**, the highest aviation honor of the American Society of Mechanical Engineers, was awarded on September 3 to John K. Northrop, president of Northrop Aircraft, Inc., Hawthorne, California. The medal, awarded every third year, was presented to Mr. Northrop "for his originality and vision in engineering of military and commercial airplanes, and particularly for his development of a successful flying wing."

**General Motors Corporation** on September 20 received the first annual Distinguished Service Award to be presented by the Special Devices Association, composed of some 600 Naval Reserve officers and civilians who have served in the Special Devices Center, Office of Naval Research. The 1947 award went to General Motors in recognition of "the outstanding accomplishment in its scientific programs involving rapid learning techniques and mass training." While this first presentation was made for wartime and subsequent peacetime contribution to the development of rapid training techniques, the purpose of the award is to promote peacetime advances in such training methods as a measure of national preparedness. Future recipients will be selected solely for current peacetime accomplishments.

## Colleges and Universities

A national center for medical research in the field of nutrition is being planned in Chicago under an agreement between Northwestern University and the Spies Committee for Clinical Research. As a first step toward implementing the plans, **Tom D. Spies**, associate professor of medicine, University of Cincinnati, has been named professor of nutrition and metabolism and chairman of a new department in this field at the Medical School of Northwestern. To maintain the department and to support research to be carried out under Dr. Spies the Spies Committee will grant to the University at least \$150,000 annually for 5 years. Dr. Spies, who is known for his work with synthetic folic acid, will continue to direct

the University of Cincinnati studies in nutrition at Hillman Hospital, Birmingham, Alabama, organized by him in 1937.

**Western College for Women**, Oxford, Ohio, will dedicate its new \$400,000 science building October 11. The new building, completed late in the spring, is now housing the Departments of Biology, Chemistry, Mathematics, Physics, and Psychology. The basement is devoted to a psychology lecture room and laboratory, animal and storage rooms, and physics laboratories for work in X-ray, radiation, glass-blowing, electronics, mechanics, and photography. Offices, classrooms, biology and botany laboratories, additional physics rooms, a greenhouse with a sunken aquarium, and the science library of 26,000 volumes occupy the first floor, while on the second floor are chemistry and biology laboratories, balance room, bacteriology laboratory, preparation room, and a physiology, histology, and embryology laboratory. Two motor control boards provide the necessary electricity for the equipment used. A special deck on the roof of the building serves as an observation platform for classes in meteorology and astronomy.

**The University of Rochester** has received from Mr. and Mrs. Ernest L. Woodward, of LeRoy, New York, a large residence and 64 acres of land together with funds for remodeling the estate into a rehabilitation hospital for children suffering from cerebral palsy. New York State has appropriated \$150,000 toward the hospital, which will be operated by the University with the cooperation of the National Foundation for Infantile Paralysis, the day clinic of the Rochester Cerebral Palsy Association, and the State Health Department. Part of the cost of technical personnel is being borne by the National Foundation under a \$292,000 grant to the School of Medicine, made last year for a 5-year program of basic research leading to improvement in the methods of treatment of children disabled by infantile paralysis and cerebral palsy. The Foundation-sponsored program is under the direction of **R. Plato Schwartz**, associate professor of orthopedic surgery at the Medical School, whose work had indicated the similarity of spasticity of muscles in infantile paralysis to that in cerebral palsy. The costs of operation and patient care will be borne by the State. In addition to research and treatment of spastic paralysis, a major aspect of the program

will be the training of personnel in any or all of the chief divisions of the plan: research at the School of Medicine, hospital care at the LeRoy unit, and work at the day clinic of the Rochester Cerebral Palsy Association.

**Case Institute of Technology** has appointed the following to its faculty: **Charles S. Bacon**, associate professor of geology and mineralogy; **Sydney D. Black**, associate professor of aeronautical engineering; **Marvin L. Granstrom**, instructor in civil and sanitary engineering; **Salvatore Cicirello**, instructor in engineering mechanics; **John E. Gilkey**, instructor in machine design; **George H. Wagner**, instructor in metallurgical engineering; **Richard G. Bauman**, instructor in physical chemistry; **Carl F. Schunemann**, instructor in electrical engineering; and **Robert P. Knupke**, instructor in mathematics.

**Rensselaer Polytechnic Institute** now offers the degrees of B.S. in vocational education and M.S. in education in order to prepare "more and better high school teachers in science, technology, mathematics, and vocational education." The New York State Department of Education and the State College for Teachers at Albany are cooperating in the program, which is under the direction of **Stanley B. Wiltse**, Department of Electrical Engineering.

**Southern Illinois University**, Carbondale, has added five new faculty members to its science departments, effective this fall. **Joseph Rafalko**, Syracuse University, and **Charles L. Foote**, Wagner College, have been named associate professors of zoology; **Arthur E. Hunter**, a recent graduate of Southern, faculty assistant in zoology; **Wilkison W. Meeks**, Western Maryland College, associate professor of physics; and **Floyd F. Cunningham**, for 17 years head of the Geography Department, State Teachers College, Florence, Alabama, associate professor and acting chairman, Geography-Geology Department.

The measuring engine of the **Yale University Observatory**, which is used to study large astronomical photographic plates, is now being utilized to check the observations made on the Einstein shift by **George Van Biesbroeck**, professor emeritus of astronomy, University of Chi-

cago, during the solar eclipse of May 20, at Bocajuva, Brazil (*Science*, May 16). While in New Haven, Prof. Van Biesbroeck is the guest of Dirk Brouwer, director, Yale Observatory.

The Einstein shift may be detected during a solar eclipse when the effect of the sun's mass causes a curvature in the path of light coming from the stars by which a star's image is displaced away from the center of the sun by a slight amount. The phenomenon was first tested by Eddington in 1919 and has since been tested by many astronomers. Most of the results have confirmed the Einstein theory, but the amount of the shift has differed appreciably in various expeditions. Prof. Van Biesbroeck improved over previous methods by photographing two points in the sky simultaneously, the star field surrounding the sun and a distant star field brought into the camera by a reflection device. In August he made a second trip to Brazil to photograph the same star field during the night.

**The Long Island College of Medicine** is now authorized to confer the degree of Doctor of Medical Science, following the Board of Trustees' approval of the expansion of teaching activities to include graduate training in psychiatry, which is the first full-time, long-term graduate course to be offered by the College. The new program in psychiatry is already in progress under the direction of **Howard W. Potter**, professor of psychiatry. The training is being given in cooperation with the Veterans Administration Program for training doctors who served in Veterans Administration hospitals and clinics.

### Industrial Laboratories

The new contact sulfuric acid works of the **E. I. du Pont de Nemours and Company, Inc.**, located 14 miles from Richmond at James River, Virginia, has begun operations. Du Pont's newest manufacturing unit, which is operated by the Grasselli Chemicals Department, makes sulfuric acid for use by industries in the Richmond area.

**M. Vincent O'Shea, Jr.**, formerly executive vice-president, O'Sullivan Rubber Company, president, Robert Teller Sons & Dorner Company, and president, Rosemarie de Paris, Inc., has been appointed administrative vice-president of **Merck & Company**, Rahway, New Jersey.

**R. C. Mason**, on leave of absence for the past year from the atomic energy project, Oak Ridge, Tennessee, has been named manager, Electro-Physics Department, Westinghouse Research Laboratories. Dr. Mason succeeds **Gaylord W. Penney**, who has been appointed Westinghouse professor of electrical engineering at Carnegie Institute of Technology.

**William H. Doherty**, radio development engineer, Bell Telephone Laboratories, New York City, has recently left for Rome, Italy, to participate in the Rome Radio Congress commemorating the 50th anniversary of Marconi's pioneer radio experiments. Mr. Doherty will present a technical paper on radio broadcast transmitters at the Congress, which is sponsored by the Italian National Council of Research. He will also visit a number of radio stations and scientific laboratories in other parts of Europe to discuss recent advances in radio communication.

**Sterling Drug, Inc.**, has announced the formation of **Winthrop-Stearns, Inc.**, as a new subsidiary to integrate its major pharmaceutical interests in this country. The new company will conduct the business hitherto carried on by **Winthrop Chemical Company, Inc.**, organized by Sterling in 1919 and now being liquidated, as well as the pharmaceutical operations of the **Frederick Stearns & Company Division**, Detroit, organized in 1855. A similar subsidiary to take over Winthrop and Stearns' Canadian business will be formed in the Dominion as soon as legal requirements are completed. **Theodore G. Klumpp**, formerly president, Winthrop Chemical Company, has been elected president of the new **Winthrop-Stearns, Inc.**

**The Electronic Control Company**, Philadelphia, which is engaged in the design of electronic digital computing equipment, has appointed the following to its staff: **Isaac L. Auerbach**, formerly development engineer, Naval Research Laboratory; **Albert Auerbach**, Radio Corporation of America; **Gerald Smoliar**, signal engineer, Army Signal Corps; and **Joseph D. Chapline, Jr.**, formerly research associate, University of Pennsylvania, and closely associated with the application of the Differential Analyzer during the war.

**Eastman Kodak Research Laboratories** have announced the following staff additions: **Robert H. Dows**, formerly



meteorologist, Army Air Forces, will do experimental work on new photographic processes; Walter R. J. Brown, who was recently graduated from the University of Toronto, will assist in colorimetry research; and Elwood J. Hunemorder, a University of Michigan graduate, will do research in X-ray photography.

## Meetings

The National Joint Committee on Fertilizer Application will hold its annual meeting in the Hotel Stevens, Chicago, December 15, in connection with the meeting of the American Society of Agricultural Engineers. The morning program will be devoted to discussion of soil fertility and plant breeding in relation to fertilizer application and radioactive applications to agriculture, while the afternoon program will be concerned with special fertilizer placement studies. Jackson B. Hester, Department of Agricultural Research, Campbell Soup Company, Riverton, New Jersey, is chairman of the Committee.

The Fourth International Congress for Microbiology, held July 20-26 in Copenhagen under the presidency of Thorvald Madsen and with Prof. Orla-Jensen as vice-president, was attended by over 1,100 persons, 87 of whom were Americans representing various branches of microbiology. The Congress was divided into 9 sections including General Microbiology, Medical and Veterinary Bacteriology, Viruses and Viral Diseases, Serology and Immunology, Soil and Water Microbiology, Dairy and Food Microbiology, Industrial Microbiology, Variation and Mutation in Microorganisms, and Plant Pathology and Mycology. General addresses were given by C. H. Werkman (U. S.) on "Assimilation of Carbon Dioxide," F. C. Bawden (England) on "Viruses in General," Ø. Winge (Denmark) on "Yeast in Modern Genetics," and S. A. Waksman (U. S.) on "Antibiotics and Life."

At the conclusion of the Congress the Emil Christian Hansen Prize for Microbiology, consisting of a gold medal and 5,000 Danish crowns and given every three years by the Carlsberg Laboratory, Copenhagen, was presented to Dr. Waksman, the first American microbiologist to receive this award. Dr. Waksman announced that the fund attached to the award will be used to help a young Danish

microbiologist come to the United States and spend a year in the Department of Microbiology, New Jersey Agricultural Experiment Station.

The Poultry Science Association held its 36th annual meeting at Clemson College, Clemson, South Carolina, August 25-28, with 351 in attendance at the general sessions and sectional programs on Nutrition, Genetics and Physiology, Extension, Pathology, and Marketing. Awards presented at the banquet meeting, August 27, included the Borden Award of \$1,000 for outstanding research work in poultry husbandry over a period of years, to J. H. Jukes, Lederle Laboratories; the National Turkey Federation Award to V. S. Asmundson, University of California; the Poultry Science Research Prize to Paul D. Sturkie, University of New Jersey; the Association's award for outstanding poultry extension work to Fred W. Frasier, Washington State College; and the Association's Teaching Award to E. M. Funk, University of Missouri.

The Association voted to join the Institute of American Biological Societies and to hold its 1948 meeting at the Colorado State Agricultural College, Fort Collins, Colorado.

Officers elected for the coming year were: W. A. Maw, MacDonald College, Quebec, president; H. M. Scott, University of Connecticut, 1st vice-president; W. M. Insko, University of Kentucky, 2nd vice-president; and E. M. Funk, University of Missouri, secretary-treasurer. Directors elected were: R. M. Bethke, Ohio Agricultural Experiment Station; T. C. Byerly, U. S. Department of Agriculture, Beltsville, Maryland; E. W. Callenbach, Pennsylvania State College; and H. S. Wilgus, Colorado Agricultural and Mechanical College. T. C. Byerly, U. S. Department of Agriculture, Beltsville, Maryland, F. B. Hutt, Cornell University, and F. A. Hays, University of Massachusetts, were elected Fellows of the Association.

## Recent Deaths

Theodore J. Becker, pharmacologist, Sterling-Winthrop Research Institute, Rensselaer, New York, died August 29.

Tine Tammes, 76, emeritus professor of genetics, University of Groningen, Netherlands, died September 20.

Elmer H. Wirth, 52, head, Department of Pharmacognosy, University of

Illinois Professional Schools, Chicago, died September 26 in Chicago.

John Robert Cochran, Jr., 73, Department of Surgery, Northwestern University Medical School, and an attending surgeon, St. Luke's Hospital, Chicago, died September 27.

Clarence Gaines Toland, 72, formerly professor of clinical surgery, University of Southern California, died October 2 of a heart ailment at his Los Angeles home.

Max Planck, 89, German physicist and Nobel Prize winner, and originator of the quantum theory, died on October 3.

Administration for Research, Volume 3 of *Science and public policy*, a series of reports by John R. Steelman, chairman of the President's Scientific Research Board, was released on October 4. In releasing the report, which analyzes a multitude of problems encountered in administering the vast scientific research and development program of the Government and offers recommendations for improvement in administration, the President stated that he is directing Federal departments and agencies engaged in important research and development activities to consider carefully the content of the report and suggested that scientists outside the Government also study the analysis and recommendations which it contains.

The report reveals the urgency of strengthening the Federal machinery in order to (1) determine broad policies, (2) allocate functions, and (3) establish liaison for purposes of closer collaboration not only within the Federal establishment but also with scientific agencies outside the Government. The specific steps proposed include: *appointment by the President of an advisory Interdepartmental Committee on Scientific Research and Development* which would consist of key government officials in charge of various aspects of the Federal research program; *creation in the Bureau of the Budget of a unit to review Federal scientific research and development programs* and thus permit the Bureau to take effective initiative in allocating functions in the field of scientific research; *designation by the President of a White House staff member who would be primarily responsible for liaison with outside scientists, learned societies, Congressional com-*

mittees, and Federal scientific agencies; and establishment of a *National Science Foundation*. With respect to the latter recommendation the report had this to say: "It is urged that the Congress establish a National Science Foundation within the administrative framework of the Federal Government. It should be located within the Executive Office of the President until such time as other Federal programs in support of higher education are established [when] consideration should be given to grouping all such activities [including the Foundation] in a single agency. The Board of the Foundation might well consist of part-time members appointed by the President, and the Director of the Foundation should be similarly chosen. Half the membership should be drawn from the personnel of Government agencies with a major role in scientific research and development, and half from among the most eminent scientists and educators outside of the Government."

Other aspects of a sound administration are discussed in subsequent pages of the 324-page report. Among them may be mentioned a lengthy chapter on scientific personnel and discussions of such matters as national security and scientific freedom, the loyalty check, and a more elastic salary system.

**The Academy of Time**, sponsored by the Benrus Watch Company and located at 200 Hudson Street, New York City, has recently released its first annual report, which was prepared by Julian Lazrus, secretary of the Academy. Since its creation in 1946 as a nonprofit organization, the Academy has provided funds to 9 universities for the scientific study of time. At American University, Ben L. Summerford, Jr., has been working on a project concerned with the relation of time to painting; the funds at Bradley University provided an undergraduate scholarship to William V. Hale, who combined watchmaking with general work leading to a B. S. degree; the recipient at Fordham University was Ruth King, whose project involved the measurement of travel time of elastic waves in the New York Area; at the University of Chicago, Leonard J. Tolmach has been investigating the isotopic ratios of lead in meteorites; at Harvard University, Carl A. Bauer's project is also related to the study of meteors; at Oklahoma A & M, H. G.

Thuesen, a professor at the College, has designed and constructed a time recorder of great accuracy; Kees Bol, at Stanford University, is working on the determination of the speed of light in empty space; and at the University of Vermont, Konrad H. Stokes is studying springs in timepieces. The recipient of funds allocated to the University of Minnesota had not been selected at the time the report was prepared. The Academy aims eventually to become a clearing house for all kinds of information on time and time keeping.

**Foster D. Snell, Inc.**, consulting chemists and engineers, are now settled in their new quarters, a 10-story building located at 29 West 15th Street, New York 11, New York.

**The program at the Hayden Planetarium**, New York, this month, entitled "Autumn Skies," will feature a realistic preview of the Orionid meteor shower, which is scheduled to occur October 22. The shower will occur when the earth passes near the orbit of the famous Halley's Comet, its gravitational pull attracting some of the debris left by the Comet and thus creating meteors. If good "seeing" prevails on October 22, observers will witness a spectacular display. Those unable to watch the real shower may witness it at the Hayden Planetarium, along with many other attractions, each weekday at 2:10, 3:40, and 8:30 P.M., and on Saturdays, Sundays, and Holidays at 10:40 A.M. (Saturdays only), 1:40, 2:40, 3:40, and 8:30 P.M.

**A series of 6 lectures on "Modern Psychiatry"** will be given in the Town Hall auditorium, 123 West 43rd Street, New York City, beginning Monday, October 20, at 5:30 P.M. The lectures, given under the auspices of the Town Hall Short Course Division, are as follows: October 20, "What Is Mental Health?" Carl Binger, associate professor of clinical psychiatry, Cornell Medical College, and editor, *Psychoanalytical Quarterly*; October 27, "The Psychiatric Implications of Immaturity," Edward A. Strecker, head, Department of Psychiatry, University of Pennsylvania, and staff neurologist, Pennsylvania, Philadelphia, and Germantown Hospitals; November 3, "What Is a Neurosis?" Franz Alexander,

director, Chicago Institute of Psychoanalysis, and associate professor of psychiatry, University of Illinois; November 10, "The Psychology of Middle-Aging," Roy R. Grinker, chairman, Department of Neuro-Psychiatry, Michael Reese Hospital, Chicago; November 17, "What Psychotherapy?" Thomas A. C. Rennie, attending psychiatrist, New York Hospital, and associate professor of psychiatry, Cornell University Medical College; and November 24, "Mental Health and World Citizenship," Frank Fremont-Smith, The World Federation for Mental Health, vice-president for the United States.

**The Sugar Research Foundation**, New York City, has recently acquired from the estate of Charles A. Browne, former staff member, Bureau of Agriculture and Industrial Chemistry, U. S. Department of Agriculture, and historian, American Chemical Society, one of the most comprehensive specialized libraries in existence on the subject of sugar. The collection, which includes more than 200 volumes and 750 bulletins and reprints with many rare and out-of-print works in several foreign languages, will be maintained as the Charles A. Browne Memorial Library at the Foundation's office, 52 Wall Street, and may be consulted for reference or research by students and those having an interest in the subject.

## Make Plans for—

**Electrochemical Society**, Fall Convention, October 15-18, Boston.

**Society of Rheology**, October 30-31, New York City.

**American Institute of Electrical Engineers**, Midwest General Meeting, November 3-7, Chicago, Illinois.

**American Institute of Chemical Engineers**, November 9-11, Detroit, Michigan.

**American Association for the Advancement of Science**, 114th Meeting, December 26-31, Chicago, Illinois.



# COMMENTS

## by Readers

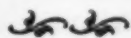
In a recent communication to this column (*Science*, August 5, p. 127) Drs. Dicker and Heller critically reviewed a recent paper of the writer dealing with the creatinine, inulin, and hippurate clearance of the rat (*Amer. J. Physiol.*, 1947, 148, 87). It was their belief that (1) the preliminary and very brief (less than 5 minutes) ether anesthesia given to the rats preceding our clearance studies, (2) handling of rats during the clearance, (3) withdrawal of 1.0-1.75 cc. of blood from the rats before the clearance, and (4) the possible variation of the blood creatinine during a possible two-hour collection period, all tended to give us results which might not be comparable to those obtained by Drs. Dicker and Heller, who employed collection methods which they believed to be more physiological.

If factors (1), (2), and (3) above were operating in our clearance studies, they acted as the authors themselves have stated (*J. Physiol.*, 1945, 103, 449), namely, to depress renal clearances. This, then, makes it difficult to understand why our average inulin clearance (19.1 cc.) at our lowest rate of urine flow was approximately the same as the average inulin clearance (21.06 cc.) of all of their clearances and why our average inulin clearance (41.1 cc.) at a high rate of urine flow was 90 per cent higher than theirs. The same discrepancy holds for their and our rates of renal plasma flow. In other words, if our technique supposedly depressed clearances, thus making them different than theirs, why are our clearances so much higher?

Concerning the fourth factor (the creatinine variation), we found, in preliminary determinations taken every 15 minutes during the collection period, that the blood creatinine remained relatively unchanged. Drs. Dicker and Heller assume that we conducted a two-hour collection because of small urine collections. We stated in our paper that the two-hour collection was designed to avoid the necessity of making clearance calculations on total collection volumes which might not exceed 0.07 cc. of urine, as occurred in some

of Dicker and Heller's experiments. We further stated, and still believe, that their clearances were erroneously low because of possible urine losses attending such small collections.

Drs. Dicker and Heller are referred to the clearance results of the rat as given by Drs. Braun-Menendez and Chiodi (*Rev. Soc. Arg. Biol.*, 1946, 23, 314). In this independent study of inulin and diodrast clearances of the rat, clearances were obtained by a technique differing from ours. Nevertheless, Dr. Braun-Menendez has informed me (as a review of his article will also demonstrate) that his clearances were almost identical with ours. Furthermore, both he and Dr. Chiodi were convinced that their clearance values varied with the urine flow. (MEYER FRIEDMAN, Mount Zion Hospital, San Francisco, California.)



In the years to come American scientists will presumably wish to participate actively in international conferences, some of which may be called on fairly short notice. The story that follows may serve to illustrate the kinds of obstacles that one may encounter because of passport difficulties. We must find ways of eliminating obstacles of this sort.

Early in August I received an official confirmation of a provisional invitation for me to attend a three-day conference called for September 11-13 by the Committee on Science and Its Social Relations (CSSR). This confirmation was in the form of a telegram from Dr. F. J. M. Stratton, chairman of the CSSR and also secretary of the International Council of Scientific Unions (of which the CSSR is a committee).

Certain preliminaries had to be taken care of, and, on August 18, I presented in person at the office of the Passport Division of the State Department in Washington, D. C., a fully-documented passport application. A passport that had originally been issued to me in 1938, and which

was recalled as a matter of routine in 1941, was on file in Washington. The clerk who received my application assured me that my passport would be issued within a week. I informed him that I was making air reservations to leave September 6 or 7.

Accompanying the passport application was an official personal letter of endorsement from Dr. Detlev W. Bronk, chairman of the National Research Council, in which he requested the issuance of a special passport. In this letter Dr. Bronk pointed out that as a part of this trip to Europe I would also stop in Paris at UNESCO Headquarters, a visit that was highly desirable for me as chairman of the NRC Committee on UNESCO.

I was preparing to leave on September 7, but when, after two weeks, no passport came, I went (again in person) to the Passport Division and inquired about the reasons for the delay. The reception given to me was kind and courteous, but I was informed by the assistant chief of the Passport Division that he could not issue a passport as long as "official clearance" had not been obtained. He promised to send me the passport himself, the moment the needed clearance would come through.

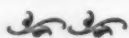
The NRC then renewed its efforts to obtain a passport in time for me to proceed to the London meeting. I informed Dr. Harlow Shapley of the unexpected delays, and he sent a telegram to the Secretary of State, urging that a passport be issued to me right away. Dr. Shapley sent this telegram in his capacity of president of the AAAS.

A personal inquiry by me to the head of the Federal Bureau of Investigation revealed that the issuing of the required clearance was wholly in the hands of the State Department.

On September 9 I talked by telephone with the assistant chief of the Passport Division, who held out hopes that a passport might come through later that day or early the next day. He offered to do everything possible to speed me on my way if the needed clearance were to come through on September 9 or 10. The "security investigation" was, however, not completed in time, and no passport was issued. On September 10 I had to telegraph to London that I would be unable to attend the London meeting.

I understand that another scientist

who was invited to attend the London meeting of the CSSR was also prevented by passport difficulties from going. The readers can judge for themselves what sort of impression our European colleagues must have formed of the importance which our State Department attaches to international scientific conferences. (BART J. BOK, associate director, Harvard Observatory.)



**Current interest in the therapeutic use of cytochrome C is widespread** as a result of a series of papers by S. Proger and associates (*Science*, October 25, 1946, pp. 389-390; *J. clin. Invest.*, 1945, 24, 864). In an attempt to provide a rational basis for their therapeutic studies, these workers drew certain conclusions which we feel are unjustified. It is understandable that such erroneous conclusions could be drawn, but it is undesirable to have them go unchallenged. The points at issue are as follows:

(1) Proger, *et al.* stated (*Science*, October 25) that "the organs normally contain considerably more cytochrome oxidase than can be activated by the cytochrome C present," based upon our data for cytochrome C content of organs (V. R. Potter and K. P. DuBois. *J. biol. Chem.*, 1943, 142, 416) and cytochrome C requirement for *in vitro* assay of cytochrome oxidase (W. C. Schneider and V. R. Potter. *J. biol. Chem.*, 1943, 149, 217). This conclusion is not permissible because the amount of cytochrome required in the assay system is not an indication of how much is needed in the cell and was not intended to be. Proger, *et al.* apparently overlooked the fact that the substrate for cytochrome oxidase is reduced cytochrome C, and that the amount of reduced cytochrome available to cytochrome oxidase is a function not only of the total cytochrome C present but of the *rate of reduction*. In the assay system this reduction is nonenzymatic and slow; hence, large amounts of cytochrome are used. In the cell the reduction is enzymatic. Thus, there is no evidence to indicate that cytochrome oxidase needs more cytochrome C than it has available in the cell.

(2) Proger, *et al.* stated in both articles cited that the cytochrome content of blood and organs was increased following cytochrome C injection. The method used was that of Potter and DuBois. This method does not permit one to decide

whether the cytochrome C has penetrated to the inside of the cells or whether it is in the blood and tissue spaces, and was not claimed to do so. In uninjected animals the blood does not contain cytochrome in significant amounts, but this is obviously not the case in the injected animals. Thus, there is no evidence that injected cytochrome C reaches the interior of the cells.

(3) Proger, *et al.* also stated that the addition of cytochrome C to homogenized tissue caused increases in oxygen uptake, and concluded that similar amounts of cytochrome C would produce comparable increases *in vivo*. But we have repeatedly emphasized the fact that when a tissue is homogenized, the cytochrome is "diluted" to an extent that depends upon a variety of factors; the extent of the dilution determines the extent of the "stimulation" when cytochrome C is added back. In the intact cells, the cytochrome C is apparently localized in the particles that contain cytochrome oxidase (W. C. Schneider, A. Claude, and G. H. Hogeboom, to be published). There has been no demonstration that the stimulation of oxygen uptake by cytochrome additions observed in homogenates can be duplicated *in vivo*, although the possibility remains that the factors which are concerned in the dilution of cytochrome in homogenates may occasionally operate *in vivo*.

(4) Proger, *et al.* (*J. biol. Chem.*, 1945, 160, 233) reported that cytochrome C administration prevented the anoxic depletion of the high-energy phosphate reservoirs of the tissues. To me, this experiment would be decisive if it could be confirmed. Unfortunately, the original experiment was done without the precautions that are necessary to preserve the phosphate compounds (G. A. LePage. *Amer. J. Physiol.*, 1946, 146, 267), and Scheinberg and Michel (*Science*, April 4, pp. 365-366) have failed to confirm the observation.

(5) There remains the final test, clinical benefit, which we are in no position to judge. We have been advised of two unpublished studies with experimental animals that gave negative results. It is desirable that the findings of Proger, *et al.* be tested by some disinterested group as soon as possible in order to prevent a great deal of unnecessary duplication of effort. At present nearly every major pharmaceutical house is undertaking to prepare cytochrome C. It is not the function of these companies to referee conflicting re-

ports, and if the demand for cytochrome C continues, it will be met. But the demand is not a proof of efficacy.

(6) Finally, it must be noted that some clinical results will stand regardless of their theoretical basis. It may be that cytochrome C will prove beneficial for reasons as yet unknown. (VAN R. POTTER, University of Wisconsin Medical School.)

[The above comment was sent by the author to Dr. Proger for criticism before being submitted for publication. Dr. Proger's reply will appear in next week's issue.]



**The unfertilized egg of an oyster is pear shaped.** In the ripe, unspawned ovary the eggs are tightly packed and compressed. The diameter of the rounded portion of an egg in the oysters kept at Woods Hole is about 40  $\mu$ . Assuming that the egg is a sphere, its volume is equal to  $\frac{4}{3}\pi R^3$ , or  $1.33 \times 3.1416 \times 8,000 \mu$ . The volume of 100,000,000 eggs is therefore only 3.3 cc. A certain correction, probably not exceeding 20 per cent, should be added to this figure to account for the void spaces between the eggs. Since the volume of the body of an adult female oyster (without the shell) varies from 15 to 25 cc., the estimated volume of eggs discharged in one spawning is not unreasonable, for it is known that the oysters lose a considerable portion of their body weight after the discharge of sex products.

In the past, too much significance was given to the number of eggs produced by females. Studies conducted by the U. S. Fish and Wildlife Service show that in Southern waters the spawning season extends from early May to October. It is therefore quite possible that the growth of the ovocytes is a more or less continuous process. This point requires further studies which are being conducted at present by the U. S. Fish and Wildlife Service. Potential fecundity of the oyster has, however, little bearing on the success or failure of reproduction, the latter primarily depending on the survival of the oyster larvae rather than on the initial abundance of spawned eggs.

I believe this brief note answers Mr. Burkenroad's criticism of my paper (*Science*, September 26, p. 290). PAUL S. GALTISOFF, U. S. Fisheries Station, Woods Hole, Massachusetts.)



# TECHNICAL PAPERS

## Citric Acid in Saliva

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Positive evidence for the occurrence of citric acid in human saliva appears to be limited to a report by Pucher, Sherman, and Vickery (5), who found 0.04–1.30 mg. per cent citric acid present in 7 specimens. Previously, Kuyper (1) and Leake (2) were unable to detect citric acid in saliva. However, they both used methods which at the time were unsuited to detect less than 2.0 mg. per cent. With slight modifications the method proposed by Perlman, Lardy, and Johnson (4) has been adapted to saliva analysis using 10-cc. quantities. Some 180 saliva specimens obtained from 15 adult men have been

ionized complex (6). Also, it has been observed in previous studies from this laboratory that citrate in practically neutral drinking fluids has a pronounced destructive action on dental tissues *in vivo* (3).

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## Wright's Hypothesis: Its Relation to Volume Growth of Tissue Cells and Mitotic Index

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In studying the length of time spent by cells in the different stages of mitosis Wright (6) first stated and made use of the following hypothesis: The fraction of the total time of mitosis spent by a cell in a given phase of mitosis is equal to the ratio of the number of cells found in that phase to the number of cells found in all phases of mitosis. According to this hypothesis it is possible to determine the time duration of all phases of the mitotic process if one can observe the duration of a single phase. For example, Wright estimated that telophase required 5 minutes for chicken-heart cells incubated at 37°C. From this time and the percentages of cells found in the various phases he established the time schedule for the mitotic cycle, the total duration of which turned out to be 34 minutes.

On the other hand, the mitotic index has been used as a measure of the rate of growth of cells in tissues (3, 4). This interpretation placed on the mitotic index assumes tacitly that the time required for mitosis,  $T$ , is constant. It can be shown that the mitotic index is proportional to the product of the time of mitosis,  $T$ , and the rate of cell division. For the important case of exponential growth of tissue volume such as occurs in liver regeneration (1, 4) and in transplantable mouse-tumor growth (2, 5) it can be shown that the mitotic index,  $m/M$ , is equal to  $(e^{\lambda T} - 1)$  in a first approximation, where  $\lambda$  is the characteristic growth constant in the tissue volume growth law,  $v = v_0 e^{\lambda T}$ . Values of  $\lambda$  have been measured for regenerating liver:  $\lambda = 1.33 \text{ days}^{-1}$  (1), and for transplantable tumors:  $\lambda = 0.37 \text{ days}^{-1}$  (5). Since  $T$  is usually of the order of 40 minutes, the product  $\lambda T$  is small, and the mitotic index is:  $m/N = \lambda T$ . This equation indicates the basis for Wright's hypothesis if one considers  $m$  as being the number of cells in any one of the stages of mitosis and  $T$  is the time spent

TABLE 1

CITRIC ACID\* IN STIMULATED SALIVA  
(Mg./100 cc.)

Case	9 A.M.	11 A.M.	1 P.M.	3 P.M.	Average
1	0.44	1.24	1.21	1.37	1.07
2	0.73	0.55	0.85	0.51	0.66
3	0.60	0.57	0.83	0.66	0.67
4	0.79	0.89	0.87	0.72	0.82
5	0.56	0.60	1.04	0.75	0.74
6	0.56	0.56	0.64	0.68	0.61
7	0.86	0.70	1.37	1.02	0.99
8	1.42	1.94	1.95	1.61	1.73
9	1.74	2.14	2.40	1.86	2.04
10	1.19	1.13	1.81	1.51	1.41
11	0.98	1.00	1.42	1.25	1.16
12	0.88	0.92	1.31	1.11	1.06
13	0.67	0.55	0.81	0.52	0.64
14	1.48	1.49	1.56	1.61	1.54
15	1.00	1.40	1.13	1.31	1.21

\* Expressed as the monohydrate.

analyzed, and the results (Table 1) afford considerably more evidence of the presence of citric acid in saliva than has been available heretofore. Paraffin-stimulated saliva was collected on three days at four different times, *i.e.* 9 A.M., 11 A.M., 1 P.M., and 3 P.M. The figures in the table are averages for three days according to time of day for each individual.

These results support the data of Pucher, *et al.* (5) and indicate that the average male adult's saliva may contain 0.50–2.00 mg. per cent citric acid. In nearly every case, results of triplicate analyses were quite consistent. In addition, samples taken every two hours throughout the day were essentially consistent, except perhaps for the slightly higher values for the 1 P.M. specimens.

Further studies are contemplated, particularly on the relation of salivary citric acid to dental erosion and dental caries. Decalcification of dental tissues by citrate ion is suggested by the observation that calcium and citrate form a soluble, slightly

by the cell in that stage. However,  $\lambda$  is a measure of the growth rate and must be assumed to be constant.

The biologic variation can be taken into account by considering the "partial mitotic index,"  $m_i/n_i = \lambda_i T_i$ . The total mitotic index becomes:

$$\frac{m}{N} = \frac{\sum m_i}{\sum n_i} = \frac{\sum \lambda_i T_i}{\sum n_i} \quad (1)$$

If  $T_i$  is the same for all cells in the tissue mass, the mitotic index becomes:

$$\frac{m}{N} = \frac{T}{N} \{n_1 \lambda_1 + n_2 \lambda_2 + \dots + n_r \lambda_r\}, \quad (2)$$

indicating again that the index is proportional to the product of  $T$  and the volume rate of growth of the tissue. The biological variation, i.e. the distribution of cells into the numbers  $n_1, n_2, n_3, \dots$  can be measured by measuring the volumes of cells in early prophase. This will give a frequency distribution of volumes which, when compared with the frequency distribution of volumes of all cells in the tissue, should give a measure of the fraction of cells in the so-called "resting stage." This fraction is of interest in exponentially growing tissue masses because it indicates the possibility that the growth constant,  $\lambda$ , for the entire tissue mass is less than that for the cells which actually contribute to the growth. Values of  $\lambda = 1.33 \text{ days}^{-1}$  lead to a volume-doubling time of 0.3 days. If a fraction of all cells are resting, the growing cells must double their volumes (on the average) in a time less than 0.3 days.

In the case of a transplantable mammary adenocarcinoma (2, 5), for small tumor volumes (less than 0.5 cc.), the volume growth of all cells can be considered approximately equal. Here Wright's hypothesis may be generalized and applied to the distribution of cell volumes to measure the rate of growth of the tumor mass. According to the hypothesis, the number of cells,  $\Delta n$ , having volumes in the interval,  $\Delta v$ , for a time,  $\Delta t$ , is given by

$$\frac{\Delta n}{N} = \frac{\Delta t}{L}, \quad (3)$$

where  $L$  is the intermitotic time and  $N$  is the total number of cells. If the frequency distribution of volumes is  $\phi(v)$  then  $\Delta n = \phi(v) \Delta v$ , and the intermitotic time is

$$t = \frac{L}{N} \int_{v_0}^v \phi(v) dv. \quad (4)$$

Here  $v_0$  is the smallest volume in the distribution, and  $t$  is a function of  $v$ . Equation 4 is the inverse of the tissue growth function,  $v = V(t)$ , and permits the determination of volume growth by means of the distribution function,  $\phi(v)$ . It can be shown that for exponential growth in the ideal case the function  $\phi(v)$  is of the form  $1/v$ . Preliminary integration of the volume distribution of cells published (2) shows that Equation 4 leads to a logarithmic relation between  $t$  and  $v$  with a characteristic constant,  $\lambda = 0.44 \text{ days}^{-1}$ , where the measured value was  $\lambda = 0.37 \text{ days}^{-1}$ . Improved techniques for measuring the cell volume distribution are being developed. The method must be tested on tumors of various ages to ascertain the possible effect of "resting cells" on the volume distribution.

It should be emphasized that this use of Wright's hypothesis applies only to a homogeneous, dedifferentiated group of cells having uniform growth rate.

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## Germination and Free Fatty Acid in Individual Cotton Seeds

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Seeds from cotton that has been exposed to wet weather in the field are likely to be lower in viability and to contain higher percentages of free fatty acids than those from seed cotton harvested without unfavorable exposure (3, 4). Similar observations have been made of cottonseed stored under conditions of high moisture or temperature (4). Conventional methods of approach to the relationship of free fatty acid content to germination would require that a sample of several hundred grams of cottonseed for the free fatty acid determination and another sample of several hundred seed for germination tests be drawn from each lot tested. When sufficient data were obtained, statistical methods could be used to study the relationship between the two variables. A second approach to the problem consists of the application of microchemical methods to the analysis for the free fatty acid content (2) of part of the nongerm portion of a single seed and the germination of the remainder of the seed.

In order to establish whether the free fatty acid content of the nongerm end of a hulled cotton seed was correlated with that of the germ end, 50 seeds were carefully peeled and cut approximately in half; each half was weighed and placed in a numbered, small, glass-stoppered Erlenmeyer flask. To each flask 5 ml. of petroleum ether (American Oil Chemists' Society, Specification H 2-41) was added and allowed to stand for about 30 minutes to soften the seeds. The seeds were then ground by means of a glass rod with a flattened end. Any material adhering to the rod was washed into the flask by means of an additional 5 ml. of the petroleum ether. The flasks were then stoppered and allowed to stand for about 16 hours with occasional shaking. After the extraction was completed, 10 ml. of neutralized alcohol containing m-cresol purple indicator was added and the mixture immediately titrated with 0.005 N alcoholic KOH. During the titration the effect of atmospheric carbon dioxide was eliminated by bubbling a stream of carbon dioxide-free air through the titration flask. The free fatty acid content is calculated as per cent oleic acid by multiplying the milliequivalents of alkali used by 28.2 and dividing the product by the weight

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the portion of kernel extracted. These values may be put in terms of the free fatty acid in the oil by multiplying by 1.5 since the kernels contain approximately one-third oil. The fatty acid content of the germ ends varied from 0.4 to 23.6 per cent and averaged 6.9 per cent; that of the nongerm ends, from 0.4 to 23.8 per cent with an average of 7.2 per cent. The correlation coefficient was 0.79, indicating a highly significant, though not by any means perfect, correlation between the free fatty acid contents of the two ends of a cotton seed. Analysis of the composited germ ends and composited nongerm ends of several hundred cottonseed showed that the nongerm end contained 39.5 per cent oil, while the germ end contained 37 per cent.

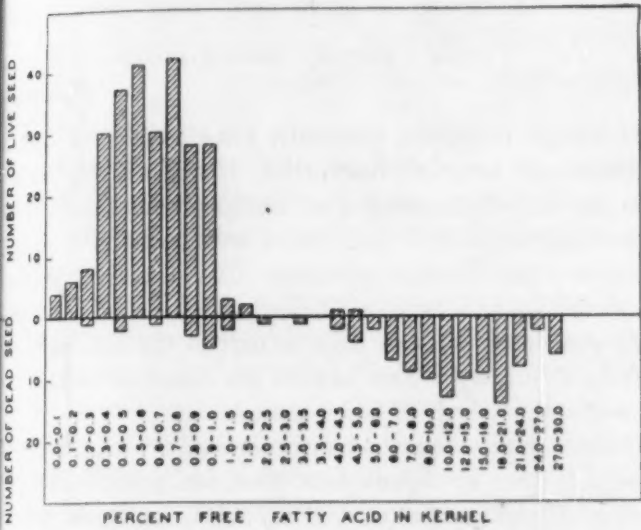


Fig. 1. Distribution of viable cottonseed according to per cent free fatty acid in kernel.

The seeds used to obtain the data plotted in Fig. 1 were selected from 10 sample lots of seed: three lots from the 1941 crop, five from the 1942 crop, and two from the 1943 crop. The seeds used were from experimental plots grown at Tifton, Georgia, Florence, South Carolina, Knoxville, Tennessee, and Baton Rouge, Louisiana, and included the following varieties: Coker's Farm Relief No. 5, Coker's 100 str. No. 1, Acala 1-13-3-1, Rowden 42A, Stoneville 37-10, and Arkansas Green Lint. The seeds were carefully hulled by hand using a razor blade. They were then cut approximately in half perpendicular to the long axis. The germ end was sterilized by dipping in a solution containing 0.25 gram of mercury dichloride dissolved in a liter of 50 per cent ethanol (1). After being rinsed in sterile distilled water the germ end was almost completely submerged, pointed end down, in sterile nutrient agar in a numbered test tube, and after being covered with a sterile cap the tube was placed in the dark to germinate. When growth above the agar, accompanied by root formation, was noted, germination was rated positive. If such growth was not observed within two weeks, the seed was rated dead.

The nongerm end was weighed, placed in a numbered flask, extracted and titrated as described above.

In Fig. 1 are shown the results obtained from 369 individual cotton seeds. Several dead seeds were found whose nongerm end contained less than 1 per cent fatty acid. These may have been seeds which were nonviable from some cause which did not produce an increase in acidity or seed in which the acidity development was higher in the germ end than represented by the analysis of the nongerm end. All seeds whose

nongerm end contained over 5 per cent of fatty acids were dead. A striking feature of the data is that so few seeds were found whose nongerm end contained from 2.0 to 4.0 per cent fatty acid. Only two seeds were found, probably indicating a rapid rise in fatty acid content in this range. Two seeds having fatty acid content in the nongerm end in excess of 4.0 per cent were found to be viable. Since these showed some discolored spots, the value for fatty acid obtained on the nongerm end is probably considerably higher than that of the germ end. The data indicate that most (over 71 per cent) of the seeds contained less than 1 per cent of free fatty acid, whereas the fatty acid content of the others ranged from 1 to 30 per cent. In the group of seeds containing less than 1 per cent the number of live seeds was about 21 times the number of dead seeds, while in that containing from 1 to 30 per cent there were 14 times as many dead as live seeds.

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Oral Efficacy of BAL in Protecting Rats Against Alloxan Diabetes

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BAL (British anti-lewisite), administered intravenously or subcutaneously as recently reported by us (2, 3), gave complete protection against the diabetogenic and lethal effect of alloxan in rats. The effective intravenous antidiabetic-dose-50 of BAL against a dose of alloxan otherwise producing diabetes in 100 per cent of injected animals was approximately 8 mg./kg. BAL was thus effective in appreciably smaller doses than cysteine (1). BAL administered intravenously or subcutaneously afforded complete and permanent protection against alloxan diabetes for 85 minutes and reduced the lethal effect of alloxan to approximately half.

Recently we have found that BAL also protects rats from alloxan diabetes by the oral route of administration, as shown in Table 1.

TABLE 1

Dose of BAL per os mg./kg.	No. of rats protected
75	0/7
110	4/7
162	5/9
237	7/7

Thus, not only is BAL effective in reducing the toxicity of alloxan, a nonmetallic compound, but it can exert its effect by the oral as well as the parenteral route.

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<sup>1</sup> With the technical assistance of Mary Ann Griffith.

# The Origin of Monocytes in the Spleen

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In recent studies on the reactions of the RES to various antigens and during infectious processes, observations were made by the writer which seem to indicate the site of origin of monocytes in the spleen. These observations were made in guinea pigs which had been inoculated with bacterial toxins or which were carriers of experimental brucellosis.

The histological study of the spleen in these cases showed peculiar reactions which were characterized by regressive or proliferative changes in the lymph follicles and by the presence of numerous mononuclear cells in the sinuses of the pulp.

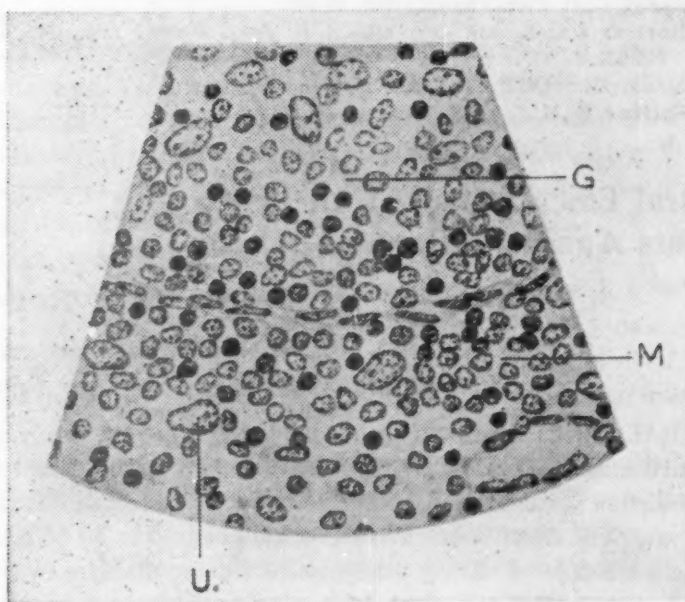


FIG. 1. Sector of a Malpighian corpuscle: G, germinal center; M, marginal zone; U, undifferentiated cell. Hematoxylin-eosin stain. (About 700 X.)

These mononuclears may be regarded as being perfectly identical with monocytes or macrophages. Generally they have a large, rounded or kidney-shaped nucleus with scarce chromatin, and slightly acidophile and well-developed cytoplasm. In the case of *Brucella* infection they appear in great numbers showing marked phagocytic activity, their cytoplasm containing red blood cells as well as cell particles and granules of hemosiderin.

What seemed particularly interesting, however, was the fact that, according to our findings, these elements apparently derive from the marginal zone of the follicles. Here numerous mesenchymal, undifferentiated cells are found proliferating, especially during the infectious process, and apparently producing the monocytes, which emigrate and fall into the lumen of the perifollicular sinuses.

Therefore, a picture similar to that observed in the lymph-nodes is found in the spleen. In fact, at the periphery of the lymph-node follicles, undifferentiated or germinal cells can be seen which are equally considered as a source of monocytes (1).

There are, then, evidences that two types of cells, with different morphological characteristics, derive from the lymph follicles or Malpighian corpuscles of the spleen, viz., cells

that are typical lymphocytes, which come from the germinal centers, and the elements we have described as monocytes which apparently originate from the marginal zone of the follicles.

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## Ultraviolet Spectrophotometric Studies in Extracts of Normal and Tumor Tissue of Human Origin

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Histologic properties frequently have a chemical correlate traceable also after cell destruction. It seems highly probable that the cell characteristics of malignant tumors should become manifest in their extracts as an increase of the nucleic acids or their cleavage products. Claude and Rothen (1), Thomas (3), and Stowell (2) suggest that nucleic acids or their protein compounds may be part of the active principle of tumor formation. Our studies are based on ultraviolet spectrophotometric analysis of tissue extracts.

Tissues were obtained at operation in 26 cases, postmortem in 4. Fourteen specimens were from malignant tumors, one each of Hodgkins' disease and leukemia, and three from benign tumors. Seven were inflammatory lymph-nodes, one an inflammatory tumor. The tissue was finely cut, suspended in saline solution (pH 7.2-7.4), and heated  $\frac{1}{2}$  hour at 65°C to inhibit enzyme action. It was centrifuged for  $\frac{1}{2}$  hour at 9,000 r.p.m. in an angle centrifuge. For ultraviolet spectrophotometric studies, a DU Beckman electric quartz spectrophotometer was used. Comparison of the optical density of the solutions was made in the same quartz cell at equal degrees of dilution. Measurements were made in steps of 10 A. between 3,100 and 2,200 A.

Normal leucocytes showed a faint indication of selective absorption at 2,600 A., but the graph looks rather S-shaped within a wave-length range between 2,800 and 2,500 A. Normal liver and endometrium are characterized by selective absorption with a peak at 2,650 A. Seven inflammatory lymph-nodes gave uniformly selective absorption with a peak in 6 cases at 2,500 A. An inflammatory tumor of the breast had an S-shaped absorption graph. Nine carcinomas showed selective absorption at 2,600 A.; a scirrhous tumor had an S-shaped graph. The height of the peak seemed in certain relation to the number of cells in the neoplastic tissues. One case, a medulloblastoma, was distinguished by two peaks at 2,550 and 2,700 A. Three lymphosarcomas and one Hodgkin's case gave similar absorption graphs with peaks at 2,600 A. Of the lymphosarcomas, one was atypical but was so clinically and histologically, diagnosis being based on tissue culture. The absorption peak in a case of lymphatic leukemia (chronic) was 2,500 A. Of the three benign tumors, two showed no selective absorption, one a low peak at 2,550 A.

Tentative suggestions can be offered regarding the selective absorption peak at 2,650 A. in normal liver and endometrium, 2,600 A. in carcinoma, and 2,500 A. in the inflammatory nodes.



From a diagnostic point of view, these differences in various pathological conditions seem of interest. The underlying causes will be the subject of further research.

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## Inactivation of Staphylocoagulase by Trypsin and Pepsin<sup>1</sup>

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Staphylocoagulase is a substance, present in filtrates of cultures of pathogenic staphylococci, which has the property of coagulating plasma. Despite its name, which would imply enzymic character, little is known of either its chemical nature or its mode of action. Walston (2) found that the active principle was not dialyzable from crude filtrates and was present in the precipitates obtained with alcohol, dilute acetic acid, or half-saturated ammonium sulfate. He also stated that the activity is destroyed by tryptic digestion. The present report is concerned with further study of the effects of trypsin and pepsin on the activity of staphylocoagulase.

Cultures of a coagulase-positive *Staphylococcus aureus* grown for 7 days in tryptic digest medium were used as the source of coagulase. After incubation, 0.5 per cent of phenol was added as a sterilizing agent, the organisms removed by

the enzyme were incubated at the appropriate pH and 37°C. for a period of 2-2.5 hours, with occasional shaking. Controls were run for each enzyme using heat-inactivated enzyme and also with no enzyme present. Before carrying out the titration of coagulase, tryptic action was checked by heating for 5 minutes at 80°C.; peptic action, by adjusting the reaction to pH 8. The preparations were cleared by centrifugation, and the coagulase titer was then determined. The activity of the enzyme preparations was checked by measuring the protein nitrogen, i.e. that precipitated by 5 per cent trichloroacetic acid, before and after the incubation.

The results are shown in Table 1. There was complete destruction of coagulase activity in all experiments with active enzymes. There was a one-dilution decrease in coagulase activity in one of the controls, otherwise no decrease in the controls.

This work bears upon the question of the enzymic or non-enzymic nature of staphylocoagulase. Its extreme resistance to thermal inactivation (1) raises some doubt as to its being a typical enzyme. The complete destruction of coagulase activity by trypsin or pepsin indicates that it contains peptide linkages hydrolyzable by these enzymes. If coagulase activity depends upon intact protein structure, it is remarkably stable when heated, since we have been able to confirm Gengou's observations and extend them by the observation that 20 minutes at autoclave temperature (120°C.) does not abolish the coagulase activity of staphylococcal culture-supernates.

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## Linkage Between the Genes for Sick Cells and the M-N Blood Types<sup>1</sup>

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It has often been pointed out that the detection of instances of linkage in man is of importance not only in an academic sense but also in order to make more precise genetic prognoses for the occurrence of anomalies and diseases (3, 4) and to institute preventive measures on the basis of early recognition of preclinical signs (2). Various methods of analyzing family data for linkage have been formulated (1, 3).

We have recently been investigating the linkage relationships of the genes for sickle cells and for the various blood groups and types. To date, 33 families have been tested. Although we found no evidence against random assortment between the gene for sickle cells and the genes for the A-B blood groups and the Rh types, we did find evidence that the gene for sickle cells is linked with those for the M-N blood types.

In order that any family may furnish information on the linkage between two genes, it is necessary that at least one parent be heterozygous for both pairs of genes. The gene for

<sup>1</sup> Studies in Human Inheritance XXXIII.

TABLE 1  
PROTEOLYTIC DIGESTION OF STAPHYLOCOAGULASE

Enzyme	pH of digestion	Coagulase titer		Percentage decrease in protein N
		Before digestion	After digestion	
Trypsin	8.7	128	0	77
"	8.7	128	0	74
"	8.7	128	0	81
"	8.7	64	0	80
Inactivated trypsin	8.7	64	64	0
None	8.7	128	64	0
Pepsin	2.0	64	0	70
"	2.0	128	0	64
"	2.0	128	0	72
Inactivated pepsin	2.0	64	64	0
None	2.0	128	128	0

centrifugation, and the clear supernates used. Coagulase activity was titrated by a serial dilution procedure in which 0.5 ml. of each dilution was mixed with an equal amount of fresh, sterile, citrated human plasma. The titer of coagulase was considered to be the highest final dilution yielding a clot filling about half the volume of the mixture at the end of 2 hours.

Commercial trypsin (Pfanstiehl) and U. S. P. pepsin (Merck) were used. Five ml. of the supernate plus 20 mg. of

<sup>1</sup> The research reported in this paper was made possible through support extended to Boston University by the Navy Department (Office of Naval Research) under contract No. N6ori-160.

sickle cells is rare enough that any sickle cell parent is almost certain to be heterozygous. Out of our 33 families there were 5 in which one parent had sickle cells and was type MN. Following the procedure of Finney (4), these may be arranged as follows:

Family	Finney Type	a	b	c	d	$\lambda$	K
7	4	3	0	0	1	6	6
8	4	1	0	0	2	3	3
11	4	1	2	1	0	0	6
17	4	0	1	0	1	-1	1
30	3	2	0	0	0	1	1
Totals.....						9	17

The total score (summation of  $\lambda$ ) is seen to be 9, with a variance (summation of K) of 17. Since the total score exceeds  $1.64 \sqrt{\text{summation of K}}$ , there is significant evidence against the hypothesis of random assortment, and we may consider that the existence of a linkage between the genes for sickle cells and for the M-N blood types has been demonstrated. As rapidly as possible we are adding to the collection of families.

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### Spleen Extract and Tumor Growth

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The relationship between the spleen and neoplastic growth has been the subject of numerous papers, only a few of which can be mentioned here (e.g. 4). Interest in the subject has been stimulated by the fact that primary carcinoma of the spleen has almost never been found and cannot be experimentally induced; nor is there growth of tumor tissue even when fragments are implanted directly into the organ (1). Metastases to the spleen from primary growths at other loci are also infrequent, and diffuse neoplastic infiltration of the spleen does not occur. The use of spleen extracts in tumor therapy has also been the subject of much controversial discussion, but that there is some definite inhibitory effect of spleen extract on tumor growth has been convincingly demonstrated by Lewisohn (2) and his collaborators in experimental animals. An aqueous extract of calf's spleen has been prepared by

the senior author and employed clinically by him for more than 18 years. He reported in 1929 (3) that two cases of Hodgkin's lesions (with and without previous X-ray therapy) showed decrease in size and softening of the nodes, but that results on other malignant growths were not encouraging. However, with improvement of techniques of extraction he has prepared a much more effective product which has been employed with decided clinical benefit, and two patients have a history of 12-13 years survival. A report of these clinical findings will be published elsewhere.

This same extract injected into mice bearing transplanted sarcoma 37 or methylcholanthrene-induced primary sarcoma produced cellular changes of a striking nature. Three concentrations were employed: "low" (8.0 grams of spleen solids/100 cc.), "medium" (15.5 grams/100 cc.) and "high" (26.5 grams/100 cc.). The difference between low and medium concentrations is merely one of an additional step in filtration. Resorption of both primary and implanted tumors was obtained, varying in percentage with the size of the tumor treated, the concentration of the extract, and the injection route employed. The best results were obtained with the medium concentration injected intraperitoneally three times daily (total daily dose, 1 cc.). The high concentration was toxic, even when injected subcutaneously; the low concentration appeared to stimulate growth. With the medium concentration, growth inhibition could be detected as early as 18 hours after the first intraperitoneal injection, and it was not necessary to resort to injection by the intravenous route. As early as 48 hours, at which time mice with transplanted tumors had received intraperitoneally 1.8 cc. of the medium concentration, almost complete degeneration of tumor cells was microscopically demonstrable. Nuclei had disappeared completely, leaving structurally intact only the cell body filled with small vacuoles. Similar phenomena were produced in about 5 days in small (5-mm. diameter), chemically induced tumors whose hosts received a total of 3.0 cc. of medium concentration spleen extract intraperitoneally. These tumors were characterized by fragmentation of nuclei and aberrant staining. With the low concentration, nuclei became greatly swollen by the end of the second day after initial injection, and this was a forerunner of increased mitotic activity. Tumors so treated grew rapidly, surpassing the dimensions of the controls. With all of the concentrations, mitosis was uninhibited as long as any viable tissue persisted. The destructive agent does not appear, therefore, to be a mitotic poison.

In Hahnemann Medical College and Hospital, three patients with malignancy and metastases (one metastatic hypernephroma and two metastatic bronchogenic carcinomas) have been injected with the Watson spleen extract (medium concentration) intravenously and intramuscularly, twice daily for 12 weeks—a total daily dose of 5-6 cc. There is definite improvement in the general health of all these patients and inhibition of progress of their tumors as revealed by Roentgen studies, made at regular intervals. Detailed clinical findings will be reported at a later date.

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# IN THE LABORATORY

## Stereotaxic Apparatus for Operations on the Human Brain<sup>1</sup>

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Exposure of subcortical areas usually necessitates rather extensive operations. It seemed desirable, therefore, to adapt the stereotaxic technic for use on the human brain. This technic, employed thus far for animal experimentation only (1), permits one to insert a wire or a cannula accurately into a desired subcortical area with minimal injury to the cerebral cortex or the white matter.

The needle holder can be moved in sagittal as well as lateral directions and lowered toward the base of the skull in a direction perpendicular to the horizontal plane of the skull or, with the needle holder tilted in the frontal or sagittal plane, at other angles to the horizontal plane. The exact position of the needle in relation to the coordinates of the skull is easily determined by the millimeter scales ( $M$ ,  $\underline{M}$ ,  $M'$ ), and the angle between needle and horizontal plane by the scales on the protractors ( $P'$ ,  $P''$ ).

The preoperative preparation and operative procedure consist of the following steps:

(1) A plaster cast is prepared which fastens the ring rigidly to the shaved head in the proper position, *i.e.* parallel to the horizontal plane (determined by the inferior margin of the orbit and the upper border of the external auditory meatus on

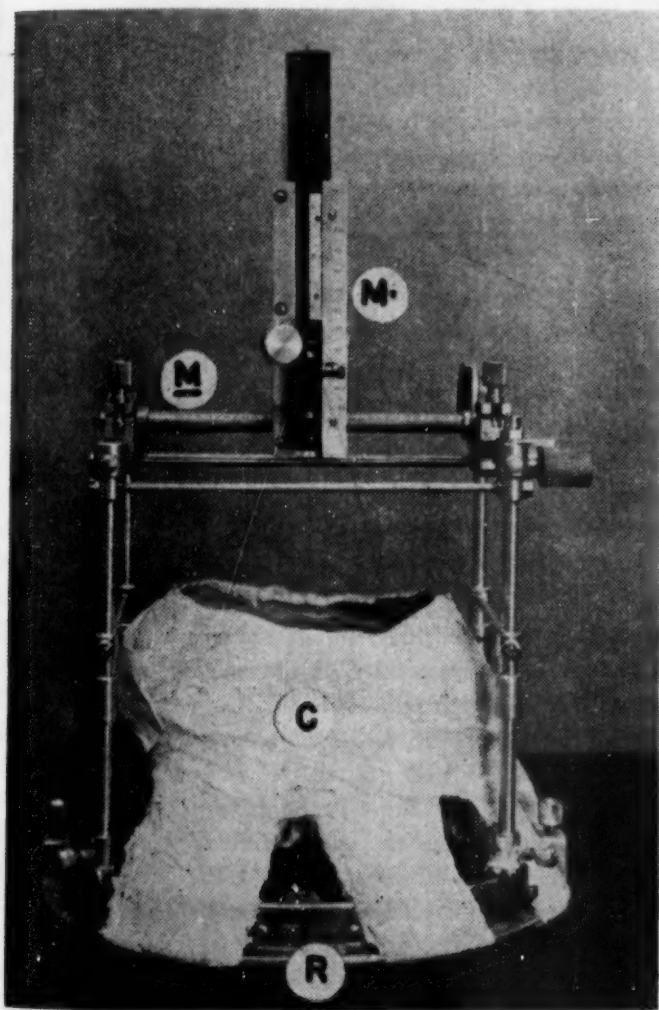


FIG. 1. Side view of stereotaxic apparatus: R = ring; C = cast of plaster of Paris;  $M$  = millimeter scale on needle holder;  $\underline{M}$  = millimeter scale for movement in sagittal direction.

Our apparatus (Figs. 1 and 2) consists of a ring (R) fixed to the skull by means of a cap of plaster of Paris (C) and a frame resting upon the ring and carrying the wire or cannula to be introduced into the brain.

<sup>1</sup> Aided by a grant from the Committee on Scientific Research, American Medical Association.

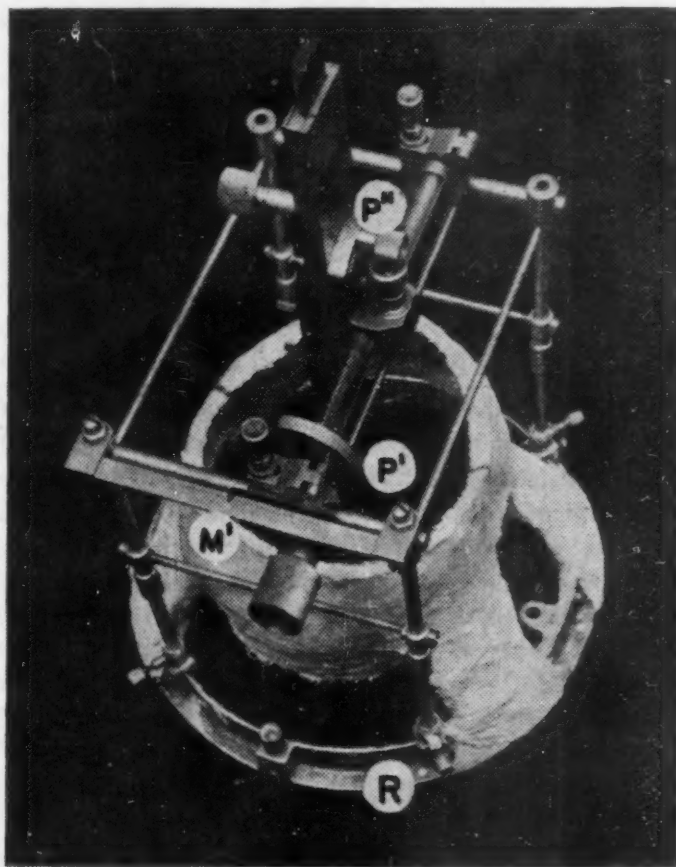


FIG. 2. Apparatus seen from above:  $M'$  = millimeter scale for movement in lateral direction;  $P'$  = protractor for tilting needle holder in frontal plane;  $P''$  = protractor (on back of needle holder) for tilting needle in sagittal plane; R = ring.

either side). After the cast has hardened, large windows are cut in its top (field of operation) and in the frontal and temporoparietal regions (for X-ray photography of the pineal body and of the region of the thalamus). It is important that the ring with the cast can be easily removed from the skull and reapplied during operation in exactly the same position as before operation.

(2) An X-ray picture is taken with the apparatus in situ

and the needle in the zero position (crossing of the interaural and midsagittal planes) before and after filling of the ventricles with air. From these photographs the coordinates of the lesion are calculated and the place of trepanation is determined.

(3) After trepanation a wire or cannula is introduced through the intact dura, a lesion is produced by thermocoagulation, fluids are aspirated or injected, etc.

This apparatus is being used for psychosurgery. In a series of patients studied in collaboration with H. Freed, lesions have been placed in the region of the medial nucleus of the thalamus (medial thalamotomy) in order to reduce the emotional reactivity by a procedure much less drastic than frontal lobotomy (2). The results so far obtained are promising. Further applications of the stereotaxic technic are under study, e.g. interruption of the spinothalamic tract in certain types of pain or phantom limb; production of pallidal lesions in involuntary movements; electrocoagulation of the Gasserian ganglion in trigeminal neuralgia; and withdrawal of fluid from pathological cavities, cystic tumors.

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### A Solution for Plasticizing Kymograph Records

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In the past, many solutions such as shellac in ethanol, resin in ethanol or isopropanol, etc. have been used to fix kymograph records. Satisfactory results were not always obtained because, as the solutions became more concentrated due to evaporation, the records were extremely sticky, did not dry rapidly, and had a glossy finish which would not photograph readily.

The solution to be described has been used for 8 months and has always given excellent results in that the records dried within 10 minutes, were never sticky, and always had a dull finish. One further advantage was the ease with which the fixing-pan was cleaned. A 10 per cent aqueous solution of sodium carbonate readily removes all traces of the dried fixative from the pan.

The plasticizing solution is composed of cellulose acetate phthalate (Eastman Kodak Co.), 10 grams; ethyl lactate, 150 cc.; ethyl acetate, 150 cc.; and ethanol or isopropanol, 700 cc. To prevent precipitation of the plastic, the solution must be mixed in the following manner: dissolve the cellulose acetate phthalate in 25 cc. of ethyl lactate and then add an equal quantity of ethyl acetate. This solution is added to half of the ethanol or isopropanol with rapid stirring. Some precipitation of the plastic may occur at this point, but the addition of another 25 cc. each of ethyl lactate and acetate will redissolve the precipitate. Add the remainder of the alcohol, ethyl lactate, and ethyl acetate in that order. Filter

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the solution by gravity through glass wool and bottle. Kymograph records are fixed in the usual manner with this finished solution.

### Yeast Autolysate: A Culture Medium for *Hemophilus influenzae*

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It is generally agreed that *H. influenzae* requires for its growth two distinct factors, the heat-labile V factor and the heat-stable X factor. Lwoff and Lwoff (5) have shown that the V factor is a coenzyme, and their observation has been confirmed by other investigators. Gingrich and Schlenk (3) reported that codehydrogenase I replaces the V factor and, in this respect, is superior to codehydrogenase II. The X factor can be replaced by crystalline beef-liver catalase according to Bass, Berkman, Saunders, and Koser (1). From the investigations of Hoagland and associates (4) as well as of Bass and co-workers (1) it is evident that in addition to these two growth factors other compounds may be required for maximal growth. Yeast is known to be rich in V factor; however, it is generally regarded to be lacking in X factor. The experiments reported below revealed that yeast autolysate supplies both growth factors required by *H. influenzae* and suggest that this substrate may be used to advantage as a culture medium and may be useful in studies on the streptomycin sensitivity of this microorganism.

The yeast autolysate (Supplement B) used in these studies was procured from Difco Laboratories. It is a filtrate of autolyzed fresh yeast and, according to Schoenlein (6), is rich in coenzyme, glutamine, cocarboxylase, and other B-vitamin factors. Difco Supplement is recommended for use in the cultivation of *Neisseria gonorrhoeae* and has been employed by Buck (2). In the present study, two lots (#388386 and #388624) proved to be equally satisfactory. For as yet unexplained reasons another lot (#386207) failed to support the growth of *H. influenzae*. The vast majority of experiments were carried out with lot #388386.

Nineteen strains of *H. influenzae* were used. Six strains were freshly isolated from the spinal fluid of patients with meningitis; the remainder were stock culture strains available in this laboratory or kindly supplied by H. E. Alexander and the Division of Laboratories and Research, New York State Department of Health. Seventeen strains belong to type b and one strain each to types a and c, respectively.

The first series of experiments was undertaken to determine the growth-promoting properties of yeast autolysate. The 19 strains of *H. influenzae* were seeded into 10 per cent yeast autolysate-brain heart infusion. All grew profusely within 24 hours in this culture medium and failed to grow entirely in brain heart infusion used as control. In view of the fact that the inoculum, which was harvested from hemoglobin-proteose peptone #3 agar, may have contained an adequate amount of X factor, serial transfers were made daily from yeast autolysate-brain heart infusion to yeast autolysate-brain heart

<sup>1</sup>The author wishes to acknowledge the technical assistance of C. F. Crotty.



infusion. Each transfer resulted in a dilution of 1:10. It was found that all strains could be maintained in this culture medium for 15 consecutive subcultures. It is noteworthy that the organisms maintained their type-specificity: specific soluble substance could be demonstrated by means of type-specific antiserum. Moreover, no changes were noted in the morphological and cultural characteristics of the organisms throughout this experiment in films and colony formation on hemoglobin-proteose #3 agar. It may be concluded, therefore, that yeast autolysate in brain heart infusion supplies the essential growth factors required by *H. influenzae*.

The growth-promoting properties of yeast autolysate in different concentrations were then studied. A strain of *H. influenzae* type b, which had been maintained in yeast autolysate-brain heart infusion for 12 consecutive subcultures, was used as inoculum of brain heart infusion containing yeast autolysate in concentrations ranging from 0.01 to 10 per cent. The seeded culture media were incubated at 37°C. The results of this experiment are summarized in Table 1.

TABLE 1  
GROWTH OF *H. influenzae* TYPE b AND PRODUCTION OF SSS IN  
BRAIN HEART INFUSION CONTAINING YEAST AUTOLYSATE

Hours of incubation	Concentration of yeast autolysate (%)				
	10	1	0.1	0.01	0
	Growth				
18	++++	++++	++	+	-
48	++++	+++	+	-	-
72	++++	+++	+	-	-
	Presence of SSS				
72	++++	++++	+++	+	-

- = no growth, no SSS; + to ++++ = various degrees of visible growth and various amounts of SSS.

It may be seen that *H. influenzae* grew profusely within 24 hours in infusion containing 1 and 10 per cent yeast autolysate while lower concentrations promoted only slight growth. Attention may be called to the fact that the strain produced type-specific substance. Similar results were obtained with several other strains of *H. influenzae*. Yeast autolysate in a concentration of 50 per cent either failed to promote growth or did so more slowly and to a lesser degree than that used in a concentration of 10 per cent.

In order to assay quantitatively the growth of *H. influenzae* in yeast autolysate-brain heart infusion, the following studies were undertaken. A strain of *H. influenzae* type b was grown in 10 per cent yeast autolysate-brain heart infusion for 24 hours. Serial dilutions (from  $10^{-1}$  to  $10^{-11}$ ) were then prepared and used for seeding of the same culture medium. In this fashion the smallest inoculum promoting visible growth was determined. It was found that growth was obtained with inocula in dilutions up to  $10^{-9}$ . Similar titrations carried out with other strains revealed that cultures of *H. influenzae* could be diluted from  $10^{-8}$  to  $10^{-11}$  and still promote growth, when used for inoculation of the 10 per cent yeast autolysate-brain heart infusion. Freshly prepared pipettes were used for each dilution. Even so, this method of titration by necessity has only limited accuracy. From the data just presented it appears to be safe to conclude that type b showed at least a 10,000,000- to 100,000,000-fold increase in this culture medium.

Preliminary studies on the comparative efficacy of yeast autolysate-brain heart infusion and hemoglobin-proteose #3 agar (Difco) revealed that growth may be obtained more rapidly in the fluid than on the solid medium, particularly if small inocula are used for seeding purposes. It appears, therefore, that the yeast autolysate medium may be superior under certain conditions to the presently employed hemoglobin-proteose #3 agar. Moreover, incubation under increased  $\text{CO}_2$  pressure is unnecessary.

In order to elucidate the question of whether the X factor is supplied by the yeast autolysate or by the brain heart infusion, 10 strains of *H. influenzae* were seeded into 10 per cent yeast autolysate-saline solution. All strains grew within 24 hours and could be maintained in this medium for 18 consecutive transfers. Since each transfer resulted in a dilution of 1:10, it seems safe to assume that X factor, which may have been present in the first inoculum, was no longer left at the end of the experiment. Therefore, yeast autolysate fulfills the growth requirements of *H. influenzae*. It seems of interest to point out that all type b strains tested produced the type-specific substance in this medium.

Yeast autolysate alone does not permit maximal growth of *H. influenzae*. This conclusion is based on the following observations: (1) A larger inoculum is necessary in order to promote growth in 10 per cent yeast autolysate-saline solution than in 10 per cent yeast autolysate-brain heart infusion. In several experiments the respective inocula were  $10^{-3}$  for yeast autolysate alone and less than  $10^{-6}$  for yeast autolysate-brain heart infusion. (2) Growth in yeast autolysate-saline solution usually is somewhat less profuse and takes place more slowly than in yeast autolysate-brain heart infusion.

On the basis of the foregoing data yeast autolysate appears to be a suitable medium for the growth of *H. influenzae*, and it seems possible that this material may be used to advantage in cultural examinations. Preliminary to such studies, experiments were carried out on the growth-promoting properties of yeast autolysate in spinal fluid procured under aseptic conditions from patients free of meningitis. Both cell count and protein content were within normal limits. It could be shown that *H. influenzae* type b grows well in 10 per cent yeast autolysate-spinal fluid and produces the type-specific soluble substance. One strain was maintained in this medium for 19 serial transfers. That yeast autolysate, indeed, may be of aid in the diagnosis of meningitis caused by *H. influenzae* is suggested by the following observation: Identical amounts of spinal fluid (no microorganisms seen on film) from a patient with clinical meningitis were seeded on hemoglobin-proteose #3 agar, blood agar, and into 10 per cent yeast autolysate-brain heart infusion. After incubation at 37°C. for 18 hours profuse cloudiness was present in the yeast autolysate medium, whereas only minute colonies were seen on the solid culture media. Anti-*H. influenzae* type b serum produced specific precipitation and/or agglutination with the yeast autolysate culture.

Determination of the sensitivity to streptomycin of strains of *H. influenzae* isolated from patients prior to, and concurrent with, chemotherapy is of practical importance. It was decided, therefore, to investigate the possible usefulness of yeast autolysate as a culture medium for such tests. Thus far 12 strains have been studied in this medium, using streptomycin in

amounts of 1 and 10  $\mu\text{g./ml.}$  The results of a representative experiment are summarized in Table 2.

It is evident that streptomycin prevents or inhibits the growth of the organism. Attention may be called to the fact that the size of the inoculum influences the degree of bacteriostasis. All 12 strains tested were inhibited by streptomycin in amounts ranging between 1 and 10  $\mu\text{g./ml.}$  This finding corresponds closely to the results obtained on solid culture media: *H. influenzae* is inhibited by 5  $\mu\text{g./ml.}$  of agar. Using yeast autolysate as the culture medium, the results may be obtained within 18 hours. Furthermore, it appears from the data presented above that such a test can be carried out even if only small numbers or organisms are available for the inoculation of the yeast autolysate medium.

TABLE 2  
BACTERIOSTATIC EFFECTS OF STREPTOMYCIN UPON *H. influenzae* TYPE b  
IN 10 PER CENT YEAST AUTOLYSATE-BRAIN HEART INFUSION

Hours of observation	10 $\mu\text{g./ml.}$	Streptomycin 1 $\mu\text{g./ml.}$	0 $\mu\text{g./ml.}$
Inoculum 0.2 ml. of undiluted culture			
18	—	++++	++++
24	—	++++	++++
48	—	++++	++++
Inoculum 0.2 ml. of 1:100 diluted culture			
18	—	++++	++++
24	—	++++	++++
48	—	++++	++++
Inoculum 0.2 ml. of 1:10,000 diluted culture			
18	—	+	++++
24	—	++	++++
48	—	++++	++++
Inoculum 0.2 ml. of 1:1,000,000 diluted culture			
18	—	—	++++
24	—	—	++++
48	—	—	++++

— = no visible growth; + to ++++ = various degrees of visible growth.

The experiments presented revealed that yeast autolysate contains the essential growth factors required by *H. influenzae*. All strains tested thus far could be grown and maintained both in 10 per cent yeast autolysate-saline solution and in yeast autolysate-brain heart infusion. It is worthy of note that these culture media promote rapid multiplication of the organism and that the resulting growth causes grossly visible cloudiness. This observation seems to be of significance, since, as stated by Hoagland and his associates (4) in 1942, "turbidity produced by growth of *H. influenzae* is rarely great, even under optimum conditions." The question remains as to the nature of the X factor present in yeast autolysate. Studies are needed to determine whether this material contains a factor identical with, or similar to, the active component in hemin or whether some other substance such as catalase acts as X factor.

From a practical point of view the demonstration of the growth-promoting properties of yeast autolysate may find several applications. It seems quite possible that yeast autolysate infusion broth may be used to advantage for the growth of *H. influenzae*, particularly for the isolation of this organism

from spinal fluid, blood, pus, etc. Preliminary studies indicate that growth may be obtained in the yeast autolysate medium more rapidly and with smaller inocula than on hemoglobin-proteose #3 agar. It is worthy of note that all type b strains grown in yeast autolysate produced the type-specific soluble substance. Studies are indicated, therefore, to determine quantitatively the amount of SSS formed in this culture medium. Such a study may yield information on the potential value of yeast autolysate cultures as immunizing antigens used in rabbits, a procedure which may be employed for the production of therapeutically effective antiserum. It has been shown, furthermore, that yeast autolysate-brain heart infusion can be used in tests designed to determine the streptomycin sensitivity of strains of *H. influenzae*.

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## A Simple Method for Changing Units

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Students and research workers frequently experience difficulty in converting a quantity from one system of units to another. The following rule, which the writer has used in his classes for several years, eliminates the uncertainty in such computations by reducing them to a routine procedure.

Rule: Write the quantity with its units in the first system. Give to each unit the coefficient 1. Substitute for each of these units its value in the second system. Reduce all numerical factors to a single coefficient, which is the numerical value of the quantity in the second system of units.

Example: Given, the coefficient of thermal conductivity of glass:

$$k = 0.00250 \frac{\text{cal. cm.}}{\text{cm.}^2 \text{ } ^\circ\text{C. sec.}}$$

Required, k in terms of B.t.u. per in. thickness per ft.<sup>2</sup> per  $^\circ\text{F.}$  per hr.

Applying the rule,

$$\begin{aligned} k &= 0.00250 \frac{[1 \text{ cal.}] [1 \text{ cm.}]}{[1 \text{ cm.}^2] [1 ^\circ\text{C.}] [1 \text{ sec.}]} \\ &= 0.00250 \frac{\left[\frac{1}{252} \text{ B.t.u.}\right] \left[\frac{1}{2.54} \text{ in.}\right]}{\left[\frac{1}{30.48} \text{ ft.}\right]^2 \left[\frac{9}{5} ^\circ\text{F.}\right] \left[\frac{1}{3,600} \text{ hr.}\right]} \\ &= 7.26 \frac{\text{B.t.u. in.}}{\text{ft.}^2 \text{ } ^\circ\text{F. hr.}} \end{aligned}$$



# A Hot-Air Apparatus Dryer for General Laboratory Use<sup>1</sup>

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A survey of the literature shows that a number of workers have felt the need of a good, quick method of drying glass apparatus (1). However, all of these dryers either have been designed for a special purpose or require some unusual techniques for building them. The design of an air dryer for general laboratory use should take into account the following requirements:

- (1) It should be constructed of easily available, commercial materials of standard design, so that construction and replacement of parts is not a burden.
- (2) It should fit well into the common arrangement of laboratory utilities.
- (3) It should be equipped with sufficient protective devices so that the usual errors in use will not result in breakdown of the equipment.

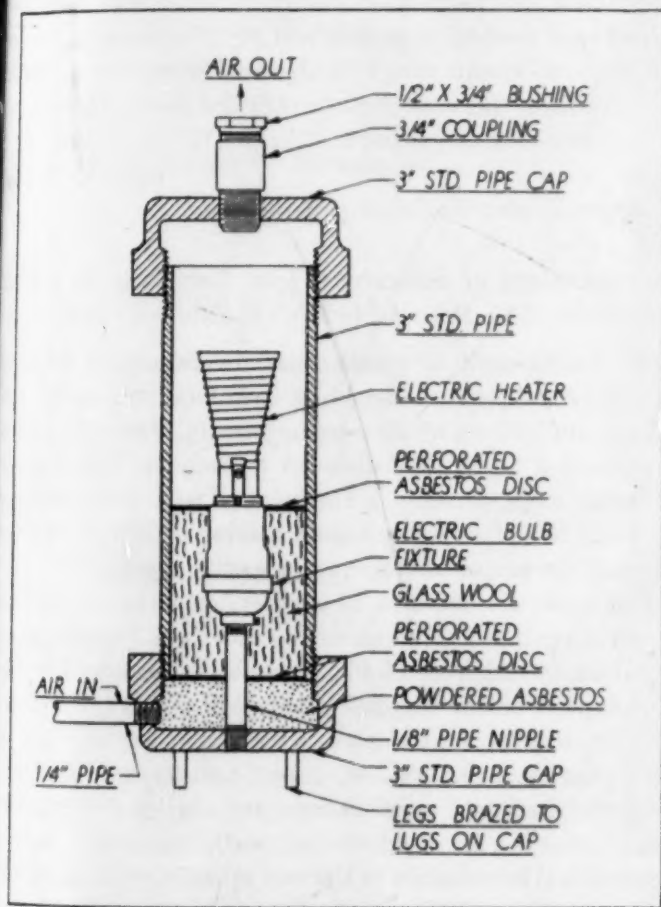


FIG. 1

The design of the equipment reported here, which has been in use in all of the student laboratories at Antioch College for the past three years, fulfills these requirements.

The air heater (Fig. 1) has an over-all height of 24 inches and should be placed at the end of a laboratory table where it can be connected directly to the utility lines that generally run through uprights, down the middle or at the back of the table. The compressed-air line is connected to the heater

<sup>1</sup> The author wishes to acknowledge suggestions on change of design made by R. A. Borden and E. L. Birch.

through a steam valve which offers easy regulation of the pressure. The electrical connection should be made with asbestos-covered wire, and the electric fixture should be porcelain to prevent a short circuit if the heater is accidentally left on without air flowing through it. The connection to the electrical utility source should be made through a standard switch box containing a safety light to show when the heater is on. The asbestos and glass-wool packing may be omitted if the air line is free from oil. When the threaded caps are not tightened to the pipe which forms the body of the heater, they are easily removed for replacement of the heating coil or packing. The unit is painted with aluminum paint or heat-resistant lacquer to prevent rusting in the usual laboratory atmosphere.

The apparatus to be dried is inverted and hung on a tubular, glass or metal support which is inserted into the coupling at the top of the heater. Although glass supports are subject to breakage, they may be made with little trouble to fit special types of drying problems and are not a source of contamination when kept clean. Metal supports may be used when special types of contamination are not objectionable. The supports are fitted to the heater by expanding the tubing over a narrow area so that it just slips inside the coupling at the top with the expanded portion resting on the nipple and a short unexpanded length extending through the nipple into the heater. The bushing is then dropped over the support and tightened until it rests firmly on the expanded portion. When glass is used, the expanded portion should be protected from the raw metal surfaces by asbestos cord.

Fig. 2 shows two designs of tubular, pyrex glass supports that have been used with success. Design A, made from 10-mm. standard-wall glass, was used for larger apparatus, where

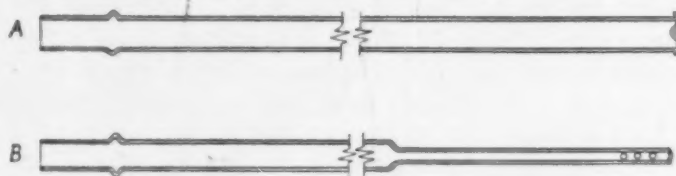


FIG. 2

considerable volume of air is needed. The bushing must be placed on the tubing before the upper end is flared. Design B, made of 5-mm. glass sealed to a 10-mm. section, allows smaller apparatus for micro and semimicro work to be dried. The sealed-off upper end kept the light pieces from being blown off the support, while the small holes in the sides furnished sufficient hot air. The length of the support may be varied at will; those used were approximately 12 inches long.

The cost of this type of drying equipment is small, and it can be installed by a plumber and an electrician. Its use by students clears drying ovens, facilitates laboratory work, and allows apparatus to be returned, dry, to the stockroom. From a cold start, the time required to obtain hot air is about 40 seconds.

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# Book Reviews

**Unified calculus.** Edward S. Smith, Meyer Salkover, and Howard K. Justice. New York: John Wiley; London: Chapman & Hall, 1947. Pp. x + 507. \$3.50.

In their effort to introduce unity into the calculus and to provide correlation with physics and mechanics, the authors have made the following noteworthy contributions: (1) the

use of the  $\frac{dy}{dx}$  notation for the derivative from the start; (2)

the interweaving of the ideas of differentiation and integration in connection with the simple polynomial functions; (3) the inclusion of applications of integration to centroids and moments of inertia with the earliest study of integration in company with the conventional applications to area, volume, liquid pressure, and work; (4) early presentation of the idea of definite integral; (5) a very clear explanation of the differential, with its applications and its relation to integration; (6) a line of choice problems on definite integrals and applications interspersed through all the chapters which deal with the formulas and methods of integration; (7) the adoption of right-handed space axes (the physicists should bless them for that!); (8) a small but adequate appendix of formulas and tables; and (9) a chapter on differential equations. While much of the text is identical with that of its excellent predecessor, there are many simplifications and clarifications which will please discriminating students and teachers. The typography is excellent, the cuts are clear and suggestive, and the somewhat smaller format which grew out of the necessity of paper conservation has not impaired the excellence of the presentation but should make the text look a little less formidable to the student. The reviewer is anxious to give it a first-hand working over with his classes this fall.

WALTER F. SHENTON

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**The chemical kinetics of the bacterial cell.** C. N. Hinshelwood. New York: Oxford Univ. Press, 1946. Pp. 284. \$6.75.

Prof. Hinshelwood, who is well known for his work in chemical kinetics, has applied some of its principles to the problems of bacterial physiology and in particular to bacterial variation. The theoretical treatment is based on the assumption that the cell is, in effect, an assembly of self-duplicating units (which the author identifies with enzymes), and that the pattern of these units determines the pattern of cellular characteristics. Much of the experimental material was obtained in the author's laboratory. The possibility that the self-duplicating entities are enzyme-forming units rather than enzymes is unfortunately not considered, although this would leave many of the formal developments unchanged. The consequences of competition among different types of self-duplicating units are also ignored; this is a more serious omission with respect to the validity of the kinetic derivations.

There is an extensive discussion of mutation and selection as possible alternatives to the mechanism proposed, and of the results of combining them with this mechanism. It is a pity that

the author did not clearly emphasize two important points: that the ability to adapt by a biochemical mechanism seems to require the presence of a specific gene, and that such a mechanism furnishes a key to the fundamental problem of the relation between genotype and phenotype.

It is surprising to find only one reference to the fundamental work on adaptive enzymes by Spiegelman and none to the important studies of the "killer" character by Sonneborn. Selection and the evolution of populations are discussed without reference to the contributions of Lotka, Volterra, DeLürick, and Luria. Finally, a book on the kinetics of self-duplicating units should include some mention of Darlington and Sewall Wright, who first called attention to the importance of such units for physiological genetics.

With regard to some of the experimental material cited, it is regrettable that adaptation to carbohydrates was studied by the awkward method of growth and lag measurements rather than the well-known direct biochemical procedures. Despite these criticisms, this book must be regarded as required reading for the general microbiologist and the theoretical biologist.

JOHN M. REINER

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**The technology of adhesives.** John Delmonte. New York: Reinhold, 1947. Pp. viii + 516. (Illustrated.) \$8.00.

The development of plastics has revolutionized adhesive technology and has broadened its usefulness into many new fields of applications which were previously either unknown or were handled by entirely different techniques. This widened industrial scope presents a complicated and often confused picture to the adhesive consumer, making it difficult to select critically the proper adhesive for a specific application.

This book, divided into 20 chapters covering all the main classes of synthetic resins as well as other well-known types of adhesives, should do much to clear up this situation. There are also chapters on the theories of adhesive action and their application to important classes of materials such as wood, organic plastics, metal, rubber, paper, textiles, and inorganic materials; tests and specifications are also described. After each chapter is a list of references, mostly to patents; much of the technical information in the text appears to be taken from patent teachings without any indication as to whether the patent claims have been substantiated by the author.

There are very few illustrations for the size of the book. More pictures demonstrating gluing equipment, techniques, and important applications would be of considerable aid to readers with little experience in the field.

The book is well written and well organized and should be very helpful to anyone connected with bonding problems in any way. It would be a valuable refresher and reference work for the expert and also serve as an up-to-date treatise for both the fabricator and layman.

J. M. GRIM

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